

INVENTOR SEARCH

=> fil capl; d que 11; d que 145
 FILE 'CAPLUS' ENTERED AT 11:10:12 ON 14 DEC 2006
 USER IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 14 Dec 2006 VOL 145 ISS 25
 FILE LAST UPDATED: 13 Dec 2006 (20061213/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>
 'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L1 1 SEA FILE=CAPLUS ABB=ON US2003-661458/APPS

L2 141 SEA FILE=CAPLUS ABB=ON PACE G7/AU
 L3 11003 SEA FILE=CAPLUS ABB=ON SMITH M7/AU
 L5 1 SEA FILE=REGISTRY ABB=ON MORPHINE/CN
 L6 1 SEA FILE=REGISTRY ABB=ON FENTANYL/CN
 L7 1 SEA FILE=REGISTRY ABB=ON SUFENTANYL/CN
 L8 1 SEA FILE=REGISTRY ABB=ON ALFENTANYL/CN
 L9 1 SEA FILE=REGISTRY ABB=ON OXYMORPHONE/CN
 L10 1 SEA FILE=REGISTRY ABB=ON HYDROMORPHONE/CN
 L11 1 SEA FILE=REGISTRY ABB=ON OXYCODONE/CN
 L12 31087 SEA FILE=CAPLUS ABB=ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)
 L13 1073 SEA FILE=CAPLUS ABB=ON L11
 L14 12914 SEA FILE=CAPLUS ABB=ON OPIOIDS/CT
 L15 1209 SEA FILE=CAPLUS ABB=ON L14(L) KAPPA/OBI
 L16 12944 SEA FILE=CAPLUS ABB=ON L14(L) MU/OBI
 L17 56591 SEA FILE=CAPLUS ABB=ON AGONISTS/OBI
 L18 368 SEA FILE=CAPLUS ABB=ON L15(L) L17
 L19 454 SEA FILE=CAPLUS ABB=ON L16(L) L17
 L37 39125 SEA FILE=CAPLUS ABB=ON DRUG INTERACTIONS-OLD, NT/CT
 L38 4450 SEA FILE=CAPLUS ABB=ON DRUG DELIVERY SYSTEMS-OLD/CT (L) COMB7/OBI
 L39 16989 SEA FILE=CAPLUS ABB=ON COMBINATION CHEMOTHERAPY/CT
 L40 5460 SEA FILE=CAPLUS ABB=ON COMB7/OBI (L) PHARMAC7/OBI
 L42 553 SEA FILE=CAPLUS ABB=ON (L12 OR L19) (L) COMB7/OBI OR COADMIN7/OBI
 BI OR CODRUG7/OBI OR CONCOMITANT7/OBI OR CONCURRENT7/OBI OR BLEND7/OBI OR MIXTURE7/OBI
 L43 82 SEA FILE=CAPLUS ABB=ON (L13 OR L18) (L) COMB7/OBI OR COADMIN7/OBI
 BI OR CODRUG7/OBI OR CONCOMITANT7/OBI OR CONCURRENT7/OBI OR

BLEND7/OBI OR MIXTURE7/OBI
 L45 5 SEA FILE=CAPLUS ABB=ON ((L42 AND L43) OR (L12 OR L19) AND (L13 OR L18) AND (L37 OR L38 OR L39 OR L40)) AND (L2 OR L3)

=> e 11.145

L210 5 (L1 OR L45)

=> fil embase; d que 181

FILE 'EMBASE' ENTERED AT 11:10:14 ON 14 DEC 2006
 Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE COVERS 1974 TO 13 Dec 2006 (20061213/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L46 83 SEA FILE=EMBASE ABB=ON PACE G7/AU
 L47 8120 SEA FILE=EMBASE ABB=ON SMITH M7/AU
 L48 53452 SEA FILE=EMBASE ABB=ON MORPHINE/CT
 L49 26736 SEA FILE=EMBASE ABB=ON FENTANYL/CT OR FENTANYL CITRATE/CT
 L50 4395 SEA FILE=EMBASE ABB=ON SUFENTANYL/CT OR SUFENTANYL CITRATE/CT
 L51 4482 SEA FILE=EMBASE ABB=ON ALFENTANYL/CT
 L52 805 SEA FILE=EMBASE ABB=ON OXYMORPHONE/CT
 L53 2957 SEA FILE=EMBASE ABB=ON HYDROMORPHONE/CT
 L54 3754 SEA FILE=EMBASE ABB=ON OXYCODONE/CT
 L72 493 SEA FILE=EMBASE ABB=ON L54(L) (CB OR IT)/CT
 L80 10397 SEA FILE=EMBASE ABB=ON (L48 OR L49 OR L50 OR L51 OR L52 OR L53) (L) (CB OR IT)/CT
 L81 5 SEA FILE=EMBASE ABB=ON (L46 AND L47) OR (L80 AND L72 AND (L46 OR L47))

=> fil drugu; d que 196

FILE 'DRUGU' ENTERED AT 11:10:15 ON 14 DEC 2006
 COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE LAST UPDATED: 11 DEC 2006 <20061211/UP>
 >>> DERMENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
 >>> THESAURUS AVAILABLE IN /CT <<<

L5 1 SEA FILE=REGISTRY ABB=ON MORPHINE/CN
 L6 1 SEA FILE=REGISTRY ABB=ON FENTANYL/CN
 L7 1 SEA FILE=REGISTRY ABB=ON SUFENTANYL/CN
 L8 1 SEA FILE=REGISTRY ABB=ON ALFENTANYL/CN
 L9 1 SEA FILE=REGISTRY ABB=ON OXYMORPHONE/CN
 L10 1 SEA FILE=REGISTRY ABB=ON HYDROMORPHONE/CN
 L11 1 SEA FILE=REGISTRY ABB=ON OXYCODONE/CN

L85 2 SEA FILE=DRUGU ABB=ON PACE G7/AU
 L86 1100 SEA FILE=DRUGU ABB=ON SMITH M7/AU
 L87 9457 SEA FILE=DRUGU ABB=ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)
 L88 269 SEA FILE=DRUGU ABB=ON L11
 L89 19705 SEA FILE=DRUGU ABB=ON MORPHINE/CT
 L90 11240 SEA FILE=DRUGU ABB=ON FENTANYL/CT
 L91 2280 SEA FILE=DRUGU ABB=ON SUFENTANYL/CT
 L92 2680 SEA FILE=DRUGU ABB=ON ALFENTANYL/CT
 L93 252 SEA FILE=DRUGU ABB=ON OXYMORPHONE/CT
 L94 866 SEA FILE=DRUGU ABB=ON HYDROMORPHONE/CT
 L95 986 SEA FILE=DRUGU ABB=ON OXYCODONE/CT
 L96 9 SEA FILE=DRUGU ABB=ON (L85 AND L86) OR ((L85 OR L86) AND (L87 OR L89 OR L90 OR L91 OR L92 OR L93 OR L94) AND (L88 OR L95))

=> fil wpi; d que 1110; d que 1123

FILE 'WPI' ENTERED AT 11:10:16 ON 14 DEC 2006
 COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE LAST UPDATED: 8 DEC 2006 <20061208/UP>
 MOST RECENT THOMSON SCIENTIFIC UPDATE: 200679 <200679/DW>
 DERMENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> YOU ARE IN THE NEW AND ENHANCED DERMENT WORLD PATENTS INDEX <<<

>>> FOR DETAILS ON THE NEW AND ENHANCED DERMENT WORLD PATENTS INDEX

PLEASE VISIT:

http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

FOR A COPY OF THE DERMENT WORLD PATENTS INDEX STN USER GUIDE,

PLEASE VISIT:

http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE

<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE

http://www.stn-international.de/stndatabases/details/ipc_reform.html and

<http://scientific.thomson.com/media/scpoff/ipcidwpi.pdf>

>>> FOR DETAILS ON THE NEW AND ENHANCED DERMENT WORLD PATENTS INDEX

PLEASE SEE

http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

>>> YOU ARE IN THE NEW AND ENHANCED DERMENT WORLD PATENTS INDEX <<<

'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPI' FILE

L108 79 SEA FILE=WPI ABB=ON PACE G7/AU
 L109 2413 SEA FILE=WPI ABB=ON SMITH M7/AU
 L110 1 SEA FILE=WPI ABB=ON L108 AND L109

L108 79 SEA FILE=WPI ABB=ON PACE G7/AU
 L109 2413 SEA FILE=WPI ABB=ON SMITH M7/AU

L111 3147 SEA FILE=WPI ABB=ON MORPHINE/BI, ABEX OR FENTANYL/BI, ABEX OR ALFENTANYL/BI, ABEX OR SUFENTANYL/BI, ABEX OR OXYMORPHONE/BI, ABEX OR MR2593/BI, ABEX OR MR2 2593/BI, ABEX OR HYDROMORPHONE/BI, ABEX

L112 4 SEA FILE=WPI ABB=ON OXYCODONE7/CN
 L113 431 SEA FILE=WPI ABB=ON L112/DCR
 L114 4 SEA FILE=WPI ABB=ON (RABAO0/SDCN OR RACDH7/SDCN OR RAOFCO/SDC N OR RO6854/SDCN OR R16303/SDCN OR 103043-1-0-0/DCSE OR 103043-1-1-0/DCSE OR 103043-1-2-0/DCSE OR 758270-1-0-0/DCSE)

L115 435 SEA FILE=WPI ABB=ON L114 OR L113
 L116 513 SEA FILE=WPI ABB=ON OXYCODONE/BI, ABEX
 L117 198 SEA FILE=WPI ABB=ON MU OPIOIDS/BI, ABEX
 L118 166 SEA FILE=WPI ABB=ON KAPPA/BI, ABEX (1W) OPIOIDS/BI, ABEX
 L119 12146 SEA FILE=WPI ABB=ON B14-L01/MC OR C14-L01/MC
 L120 100 SEA FILE=WPI ABB=ON L117 (2A) AGONISTS/BI, ABEX OR (L117 AND L119)

L121 102 SEA FILE=WPI ABB=ON L118 (2A) AGONISTS/BI, ABEX OR (L118 AND L119)

L122 486502 SEA FILE=WPI ABB=ON (M782 OR P867)/MO, M1, M2, M3, M4, M5, M6 OR A61K045/IPC OR (B12-C09 OR C12-C09 OR B14-S09 OR C14-S09)/MC
 L123 4 SEA FILE=WPI ABB=ON (L108 OR L109) AND (L111 OR L120) AND (L115 OR L116 OR L121) AND L122

=> e 1110.1123

L211 4 (L110 OR L123)

=> fil medl; d que 1163

FILE 'MEDLINE' ENTERED AT 11:10:19 ON 14 DEC 2006

FILE LAST UPDATED: 13 Dec 2006 (20061213/UP). FILE COVERS 1950 TO DATE.

In preparation for the annual MEDLINE reload, the National Library of Medicine (NLM) has suspended delivery of regular updates as of November 15, 2006. In-process and in-data-review records will resume delivery on November 21, 2006, and will continue to be added to MEDLINE until December 17, 2006.

On December 17, 2006, all regular MEDLINE updates from November 15 to December 16 will be added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R)) and 2007 tree numbers.

The annual reload will be available in early 2007.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L144(94) SEA FILE=MEDLINE ABB=ON PACE G7/AU
 L145(10732) SEA FILE=MEDLINE ABB=ON SMITH M7/AU
 L146(0) SEA FILE=MEDLINE ABB=ON L144 AND L145
 L147(28104) SEA FILE=MEDLINE ABB=ON MORPHINE/CT
 L148(10382) SEA FILE=MEDLINE ABB=ON FENTANYL-NI/CT
 L149(294) SEA FILE=MEDLINE ABB=ON OXYMORPHONE/CT
 L150(704) SEA FILE=MEDLINE ABB=ON HYDROMORPHONE/CT
 L151(540) SEA FILE=MEDLINE ABB=ON OXYCODONE/CT
 L152(124991) SEA FILE=MEDLINE ABB=ON LUNG DISEASES, OBSTRUCTIVE-NI/CT
 L153(5936) SEA FILE=MEDLINE ABB=ON BRONCHIECTASIS-NI/CT

L154(57086)SEA FILE-MEDLINE ABS-ON TUBERCULOSIS, PULMONARY-NT/CT
 L155(3460)SEA FILE-MEDLINE ABS-ON BRONCHOPNEUMONIA/CT
 L156(3610)SEA FILE-MEDLINE ABS-ON LARYNGITIS-NT/CT
 L157(11628)SEA FILE-MEDLINE ABS-ON SINUSITIS-NT/CT
 L158(13172)SEA FILE-MEDLINE ABS-ON PULMONARY FIBROSIS/CT
 L159(1561)SEA FILE-MEDLINE ABS-ON SARCOIDOSIS, PULMONARY/CT
 L160(113814)SEA FILE-MEDLINE ABS-ON LUNG NEOPLASMS-NT/CT
 L161(12768)SEA FILE-MEDLINE ABS-ON SLEEP APNEA SYNDROMES-NT/CT
 L162(0)SEA FILE-MEDLINE ABS-ON (L144 OR L145) AND (L147 OR L148 OR L149 OR L150 OR L151) AND (L152 OR L153 OR L154 OR L155 OR L156 OR L157 OR L158 OR L159 OR L160 OR L161)
 L163 0 SEA FILE-MEDLINE ABS-ON L146 OR L162

>> dup rem 196,1210,1211,181

FILE 'DRUGU' ENTERED AT 11:10:37 ON 14 DEC 2006
 COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'CAPLUS' ENTERED AT 11:10:37 ON 14 DEC 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE 'HELP USAGETERMS' FOR DETAILS.
 COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WP1X' ENTERED AT 11:10:37 ON 14 DEC 2006
 COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'EMBASE' ENTERED AT 11:10:37 ON 14 DEC 2006

Copyright (c) 2006 Elsevier B.V. All rights reserved.
 PROCESSING COMPLETED FOR L96
 PROCESSING COMPLETED FOR L210
 PROCESSING COMPLETED FOR L211
 PROCESSING COMPLETED FOR L81

L212 16 DUP REM L96 L210 L211 L81 (7 DUPLICATES REMOVED)
 ANSWERS '1-9' FROM FILE DRUGU
 ANSWERS '10-13' FROM FILE CAPLUS
 ANSWER '14' FROM FILE WP1X
 ANSWERS '15-16' FROM FILE EMBASE

>> d ibid ed abs 1-16

L212 ANSWER 1 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN DUPLICATE 2
 ACCESSION NUMBER: 2005-27268 DRUGU P S Full-text

TITLE: Ventilatory responses of healthy subjects to intravenous combinations of morphine and oxycodone under imposed hypercapnic and hypoxemic conditions.

AUTHOR: Ladd L A; Kam P C; Williams D B; Wright A W E; Smith M T; Mather L E

CORPORATE SOURCE: Univ. Sydney; Sigma-Pharmaceuticals; Univ. Queensland
 LOCATION: Brisbane; Melbourne, Austr.

SOURCE: Br. J. Clin. Pharmacol. (59, No. 5, 524-35, 2005) 5 Fig. 2 Tab. 37 Ref.

AVAIL. OF DOC.: CODEN: BCPHWM ISSN: 0306-5251
 Department of Anaesthesia and Pain Management, University of Sydney at Royal North Shore Hospital, St Leonards, NSW 2065, Australia. (L.E.M.). (e-mail: lmath@med.usyd.edu.au).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 2005-27268 DRUGU P S Full-text

5

AB I.v. infusions of morphine sulfate (MOR) or oxycodone HCl (OXH) or their combination decreased the hypercapnic response and VE55 (i.e., mean minute ventilation at PETCO₂ 55 mmHg) to a similar degree in a randomized, placebo-controlled, double-blind, crossover study of 12 male volunteers. There was no consistent treatment effect on the hypoxemic response. OXH was associated with drowsiness, tingling, warm feeling, itching, and nausea. These findings suggest that no unexpected or disproportionate effects are expected of MOR and OXH treatments that might impede their use in combination for pain management.

ABEX Methods 12 Male volunteers (aged 18-45 yr) randomly received 1-hr i.v. infusions of placebo, MOR (7.5, 10, and 15 mg, M7.5, M10, and M15, respectively), OXH (5, 7.5, 10, and 15 mg, O5-O15, respectively), or their combination in dose ratios of 1:2, 1:1, and 2:1, in a crossover manner. Results Subjective side-effects increased with increasing OXH doses. Drowsiness, tingling, and warm feeling were mostly mild and random, although some subjects tended to experience recurring side-effects (e.g., itching or nausea). A consistent treatment effect was not demonstrated for slope or intercept of the hypoxemic response. There was a consistent and similar decrease in slope of the hypercapnic response during all active drug treatments (DT), with general recovery after treatment. There was also a consistent decrease of VE55 during all treatments, with partial recovery after DT, but not between active DT. During DT, VE55 decreased to a mean of 74% of the respective values before DT (74%, 68%, 69%, 68%, and 61% for M15, M10/O5, M7.5/O7.5, M5/O10, and O15, respectively). After DT, mean values of VE55 were 75%, 73%, 76%, 76%, and 75% of the respective values before DT. Drug and metabolite AUC 0-120 hr were linearly proportional to dose and did not differ between drugs. Although there were differences in mean plasma drug concentrations between subjects, there were no differences between treatments during infusion; differences were found between treatments after infusion, with concentrations being directly correlated with the OXH dose. VE55 was the most sensitive ventilatory response variable for comparing the individuals and treatments in relation to drug plasma concentrations. (ABD/Y230)

L212 ANSWER 2 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN DUPLICATE 4
 ACCESSION NUMBER: 2000-12785 DRUGU P S Full-text

TITLE: Co-administration of sub-antinoceptive doses of oxycodone and morphine produces marked antinoceptive synergy with reduced CNS side effects in rats.
 AUTHOR: Ross F B; Wallis S C; Smith M T

CORPORATE SOURCE: Univ. Queensland
 LOCATION: Brisbane, Austr.

AVAIL. OF DOC.: Pain (84, No. 2-3, 421-28, 2000) 4 Fig. 24 Ref. CODEN: PAINDB ISSN: 0304-3959

SCHOOL OF PHARMACY, THE UNIVERSITY OF QUEENSLAND, ST. LUCIA, BRISBANE, QUEENSLAND 4072, AUSTRALIA. (M.T.S.). (e-mail: M.ross@pharmacy.uq.edu.au).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 2000-12785 DRUGU P S Full-text
 AB The effects of i.c.v. i.p. and s.c. oxycodone hydrochloride (Boots) and morphine hydrochloride on nociception were studied in rats. Co-administration of oxycodone and morphine produced the levels of antinociception. Behaviorally rats that received equipotent doses of either opioid alone were markedly sedated. The results suggested that co-administration of sub-analgesic doses of oxycodone and morphine could provide excellent pain relief with a reduction in opioid related CNS side effects.

6

ABEX Marked antinociceptive synergy was seen in Sprague-Dawley and Dark Agouti rats following sub-antinoceptive doses of oxycodone or morphine, irrespective of whether they were given i.c.v., i.p. or s.c. Sub-antinoceptive doses of either oxycodone or morphine alone to rats produced levels of antinociception similar to pre-dosing baseline levels. In Sprague-Dawley rats i.c.v. oxycodone at 40 nmol and morphine at 15 nmol caused a rapid onset (by 10 min) of maximum possible antinociception (MPE) which decreased relatively slowly (mean level of antinociception, greater than 50% of MPE at 3 hr). Pretreatment with naloxomazine or nor-BNI 24 hr prior to i.c.v. oxycodone 40 nmol plus morphine 15 nmol resulted in a decrease in the levels of antinociception. In Dark Agouti rats i.p. oxycodone at 571 nmol plus morphine at 621 nmol resulted in 100% MPE by 10 min. The mean levels of antinociception remained high for the 1st 2 hr of the experimental period and then decreased to 65% MPE by 3 hr postdosing. Oxycodone 571 nmol i.p. with 310 nmol morphine or oxycodone 285 nmol plus 621 nmol morphine resulted in maximum antinociception by 15 min but the duration of action was reduced to 2 hr. Co-administration of oxycodone or morphine in sub-antinoceptive doses neither strain of rat showed any adverse behavioral effects such as sedation, incontinence or catatonias. In Dark Agouti rats the ED50 doses of s.c. oxycodone and morphine were 2.8 and 8.5 mg/kg, respectively. Behaviorally rats given single s.c. morphine or oxycodone in doses larger than the ED50 were sedated. Co-administration of sub-antinoceptive doses of oxycodone and morphine produced synergistic levels of pain relief. (LL)

L212 ANSWER 3 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN DUPLICATE 6
 ACCESSION NUMBER: 1994-22863 DRUGU P S Full-text

TITLE: The antinociceptive potencies of oxycodone, noroxycodone and morphine after intracerebroventricular administration to rats.

AUTHOR: Leow K P; Smith M T

CORPORATE SOURCE: Univ. Queensland
 LOCATION: Brisbane, Australia

SOURCE: Life Sci. (54, No. 17, 1229-36, 1994) 2 Fig. 1 Tab. 20 Ref. CODEN: LIFSAK ISSN: 0024-3205

AVAIL. OF DOC.: Department of Pharmacy, The University of Queensland, St Lucia, Queensland 4072, Australia. (M.T.S.).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 1994-22863 DRUGU P S Full-text

AB In rats, i.c.v. administration of noroxycodone (NOR, Du-Pont-Merck) or oxycodone HCl (OXY, Sigma-Chemical) had a more potent antinociceptive effect than that of i.c.v. morphine HCl (MOR). Administration of i.c.v. naloxone HCl (Sigma-Chemical) abolished the antinociceptive response produced by the subsequent administration of OXY, MOR or NOR, indicating that the antinociceptive effects of these 3 drugs are mediated by opioid receptors. MOR also produced excitatory effects throughout the antinociceptive range, the severity of which was reduced, but not abolished, by prior administration of i.c.v. naloxone. As excitatory effects have not been observed in patients receiving OXY, it is unlikely that MOR contributes to the analgesic activity of OXY administered systemically.

ABEX In male Sprague-Dawley rats (250 g), the ED50 value for i.c.v. MOR was 34 nmol. Corresponding ED50 values for i.c.v. OXY and MOR were 78 and 200 nmol, respectively. Antinociceptive potencies of OXY and MOR relative to MOR, estimated using the ED50 values, were 0.44 and 0.17, respectively. After i.c.v. MOR, the antinociceptive response comprised 2 distinct phases. During phase 1, antinociception commenced at 15-30 min,

peaked at 45-60 min and decreased at 75 min. Phase 2 antinociception peaked at 90 min and decreased throughout the remainder of the 3-hr observation period. During phase 2 antinociception, rats were incontinent. Only phase 1 antinociception was observed in rats given OXY. Onset of antinociception was very rapid with peak values occurring at 7-15 min post-dosing. When MOR was administered, 2 antinociceptive phases were observed in a manner analogous to that observed after i.c.v. MOR. Time to achieve maximum antinociception was significantly shorter for OXY (9.3 min) than for MOR (31.8 min) or NOR (34.6 min). At equipotent doses, the mean duration of antinociception was significantly shorter for i.c.v. OXY (114 min) than for i.c.v. MOR and NOR (180 min). Naloxone (55 nmol) given 15 min prior to i.c.v. opioid agonist significantly reduced the antinociceptive response of the respective opioid agonist administered alone. NOR also produced allodynia, excessive facial grooming, tremor, Straub tail and myoclonic jerks. The severity of these effects was reduced but not eliminated by subsequent naloxone. Grand mal seizures then death occurred in 2 rats given 432 nmol of MOR. (SAB)

L212 ANSWER 4 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN

ACCESSION NUMBER: 2000-44276 DRUGU P S Full-text

TITLE: Incomplete, asymmetric, and route-dependent cross-tolerance between oxycodone and morphine in the Dark Agouti rat.

AUTHOR: Nielsen C K; Ross F B; Smith M T

CORPORATE SOURCE: Univ. Queensland
 LOCATION: Brisbane, Austr.

SOURCE: J. Pharmacol. Exp. Ther. (295, No. 1, 91-99, 2000) 4 Fig. 4 Tab. 29 Ref.

AVAIL. OF DOC.: CODEN: JPETAB ISSN: 0022-3565

SCHOOL OF PHARMACY, THE UNIVERSITY OF QUEENSLAND, ST. LUCIA, QUEENSLAND 4072, AUSTRALIA. (M.T.S.). (e-mail: m.smith@pharmacy.uq.edu.au).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 2000-44276 DRUGU P S Full-text

AB The antinociceptive effects of bolus i.v. or i.c.v. oxycodone HCl (OX, Tasmanian Alkaloids) or morphine sulfate (MP) were determined in OX- and MP-tolerant rats. In MP-tolerant rats, i.c.v. OX did not induce cross-tolerance whereas i.v. OX induced a low degree of cross-tolerance. In OX-tolerant rats, both i.c.v. and i.v. induced a high degree of cross-tolerance. It was concluded that after parenteral but not supraspinal administration, OX is metabolized to a mu-opioid agonist metabolite, thereby explaining asymmetric and incomplete cross-tolerance between OX and MP.

ABEX Methods Dark Agouti rats (200 g) received i.v. infusion of OX (2.5 or 5 mg/day) or MP (10 or 20 mg/day) until rats were completely tolerant followed by 12-hr washout period. OX-tolerant, MP-tolerant and drug-naïve rats received either bolus i.v. OX (79-1585 nmol) or MP (350-3504 nmol) or bolus i.c.v. OX (22-132 nmol) or MP (18-150 nmol). Results Complete antinociceptive tolerance was produced by 48 hr in naïve rats following chronic i.v. infusion of OX (2.5 mg/day) and MP (10 mg/day). Chronic i.v. infusion of OX (5 mg/day) induced tolerance in naïve, MP-tolerant and OX-tolerant rats after 72 hr, 48 hr and 8 hr, respectively. Chronic i.v. infusion of MP (20 mg/day) induced tolerance in naïve, OX-tolerant and MP-tolerant rats after 84 hr, 36 hr and 12 hr, respectively. Equipotent antinociception was produced by chronic i.v. OX and MP in doses of 2.5 mg/day and 10 mg/day, respectively, and tolerance was established over a similar time frame. In MP-tolerant rats, i.c.v. OX did not affect the dose-response curve or ED50 of i.c.v. OX, whereas

i.c.v. MP increased the ED50 of i.c.v. MP. In OX-tolerant and MP-tolerant rats, i.c.v. MP caused a rightward shift in the dose-response curve of i.c.v. MP and increased the ED50 of i.c.v. MP by 1.9-fold and 2.6-fold, respectively. Rats that received i.c.v. or i.v. MP or OX were sedated, whereas rats that received i.c.v. MP experienced urinary incontinence. In MP-tolerant rats, i.v. OX and i.v. MP increased the ED50 of OX. Similarly in OX-tolerant rats, i.v. MP and i.v. OX increased the ED50 of MP. i.v. OX produced a lower degree of tolerance in MP-tolerant rats than did i.v. MP in OX-tolerant rats (23.7% vs. 71.3%). (NK)

L212 ANSWER 5 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN

ACCESSION NUMBER: 1998-04922 DRUGU P Full-text

TITLE: The intrinsic antinociceptive effects of oxycodone appear to be K-opioid receptor mediated.

AUTHOR: Rose F B; Smith M T

CORPORATE SOURCE: Univ. Queensland

LOCATION: Brisbane, Austr.

SOURCE: Pain (73, No. 2, 151-57, 1997) 5 Fig. 33 Ref.

CODEN: PAINOB ISSN: 0304-3959

AVAIL. OF DOC.: School of Pharmacy, Steele Building, The University of Queensland, St. Lucia, Brisbane, Queensland 4072, Australia. (E-mail: marce.smith@pharmacy.uq.edu.au).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 1998-04922 DRUGU P Full-text

AB The Authors' previous studies in the Sprague-Dawley rat showed that the intrinsic antinociceptive effects of oxycodone are naloxone reversible in a manner analogous to morphine but, in contrast to morphine, oxycodone's antinociceptive effects have a rapid onset of maximum effect, comprise 1 (not 2) antinociceptive phases and are of relatively short duration. This study used a range of selective opioid receptor antagonists to identify the major class of opioid receptors mediating the intrinsic antinociceptive effects of oxycodone following its i.c.v. administration to rats. The data strongly suggested that the antinociceptive actions of oxycodone are mediated by kappa-opioid receptors, in contrast to morphine which interacts primarily with mu-opioid receptors.

ABEX A range of selective opioid receptor antagonists were given to adult male Sprague dawley rats (200 +/- 20 g). The intrinsic antinociceptive effects of oxycodone (171 nmol) were not attenuated by i.c.v. administration of (i) naloxazine (1 nmol), a μ -selective opioid receptor antagonist, or (ii) naltrindole (2.2 nmol), a δ -selective opioid receptor antagonist. In doses that completely attenuated the intrinsic antinociceptive effects of equipotent doses of the respective μ and δ -opioid agonists, morphine (78 nmol) and enkephalin-2-D-Pen-5-Pen (DPDPE, 55 nmol). Although beta-funaltrexamine (B-FNA, 4 nmol) attenuated the antinociceptive effects of oxycodone (171 nmol i.c.v.), it also attenuated the antinociceptive effects of morphine (78 nmol) and bremazocine (57 nmol; kappa-opioid agonist) indicative of non-selective antagonism. Importantly, the antinociceptive effects of oxycodone (171 nmol i.c.v.) were markedly attenuated by the prior i.c.v. administration of the selective kappa-opioid receptor antagonist, norbinaltorphimine, in a dose (0.3 nmol) that did not attenuate the antinociceptive effects of an equipotent dose of i.c.v. morphine (78 nmol). (PH)

L212 ANSWER 6 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN

ACCESSION NUMBER: 1994-27116 DRUGU P Full-text

TITLE: Serum protein binding of oxycodone and morphine.

9

fractions also increased with a decrease in temperature, and decreased with a small reduction in pH. Serum samples spiked with known OX concentrations showed a gradual decline in serum protein binding with storage time. It is concluded that disease states altering protein concentrations may affect serum protein binding of OX or MO, but that this is unlikely to alter pharmacological effects due to their normally low extent of protein binding.

ABEX Mean (and range) concentrations of total protein, albumin and AAG in blood from healthy volunteers were 74 (62-80), 44 (35-48) and 0.91 (0.55-2.4) g/l, respectively. At physiological pH and temperature, mean serum protein binding (measured by ultrafiltration) was 45.1% for OX and 35.3% for MO. Total and unbound MO and OX were measured by HPLC. A decrease in temperature from 37 to 23 deg. increased serum protein binding by 8-9% for OX and 7-10% for MO. A reduction in pH from 7.75-8.85 to 7.4 reduced serum protein binding by 4-5% for OX and 4-7% for MO. For each pH and temperature variation, serum protein binding for MO was lower than for OX and independent of drug concentration from 5 to 100 ng/ml. Storage of serum samples containing known concentrations of OX from about 45% to 39% at 4 wk. Albumin was the major binding protein for both OX and MO, with AAG accounting for only a small proportion of total binding. The bound fraction of OX and MO increased with increasing albumin and AAG concentrations, with higher binding for OX than MO. A reduction in pH to 7.4 and increase in temperature from 23 to 37 deg reduced the binding affinities (K_a) of OX and MO in serum. At each pH and temperature, K_a for MO was lower than that for OX. Binding affinities were higher for AAG than HSA for both OX and MO, and did not change with different protein concentrations. For both OX and MO, K_a was inversely proportional to HSA concentration. The fraction of OX bound to AAG increased with AAG concentration, but the % MO bound was only weakly correlated with AAG concentration. (W103/KP)

L212 ANSWER 8 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN

ACCESSION NUMBER: 1994-06523 DRUGU P Full-text

TITLE: Antinociceptive Potencies of Oxycodone (OC), Noroxycodone (NOC) and Morphine (M) After ICV Administration to Rats.

AUTHOR: Smith M T; Leow K P

CORPORATE SOURCE: Univ. Queensland

LOCATION: Brisbane, Australia

SOURCE: Clin. Exp. Pharmacol. Physiol. (Suppl. 1, 67, 1993)

CODEN: CEXPB9 ISSN: 0305-1870

AVAIL. OF DOC.: Department of Pharmacy, University of Queensland, Qld 4072, Australia.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 1994-06523 DRUGU P Full-text

AB The antinociceptive potencies of oxycodone (OC), its metabolite noroxycodone (NOC) and of morphine (M) were compared after i.c.v. administration in rats, using the tail flick latency test. Analgesic activity was demonstrated for NOC, but it was not as potent as M or OC. i.c.v. naloxone (NAL) blocked the antinociceptive effects of OC and NOC, but failed to totally eliminate the excitatory effects (allodynia, excessive grooming, tremor, Straub tail, myoclonus, etc.) elicited by i.c.v. NOC. It is thus possible that non-opioid mechanisms are involved in the excitatory effects of NOC as has been reported previously for high-dose i.c.v. M. (congress abstract).

ABEX The i.c.v. ED50 values for M, OC, and NOC were 11, 27.5 and 57 ug, respectively. Whilst antinociception (more than 50% of maximal possible effect) was noted for all doses of M tested (5 ug or higher), antinociceptive activity was noted only in rats receiving at least 40 ug

Wright A M E; Leow K P; Cramond T; Smith M T

CORPORATE SOURCE: Univ. Queensland

LOCATION: Brisbane, Australia

SOURCE: Aust. J. Hosp. Pharm. (24, No. 2, 206, 1994)

CODEN: AUNPA1 ISSN: 0310-6810

AVAIL. OF DOC.: Dept. of Pharmacy, The University of Queensland, Brisbane, Queensland, 4072, Australia.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AN 1994-27116 DRUGU P Full-text

AB The study aim was to determine the extent of serum protein binding of oxycodone (OX) and morphine (MO) in HSA and human alpha₁-acid glycoprotein (AAG). OX and MO bound primarily to HSA, although both drugs bound to AAG with a higher affinity than to albumin. A decrease in temperature or an increase in pH significantly increased the protein binding of both OX and MO. The serum protein binding of both opioids was independent of drug concentration in the therapeutic range (5-100 ng/ml), but was dependent on the protein concentration. It is unlikely that changes in serum protein concentrations associated with disease states such as renal or hepatic failure would alter the pharmacological effects of OX or MO due to the normally low extent of binding of both drugs. (congress abstract).

ABEX Methods: Serum protein binding was determined in-vitro by ultrafiltration. Binding studies were also performed using both purified HSA and AAG. Results: OX and MO bound primarily to albumin although both drugs bound to AAG with a higher affinity than to albumin. At physiological pH and temperature, the mean serum protein binding of OX and MO were 45.1% and 35.3%, respectively. A decrease in temperature (from 37 deg to 23 deg) or an increase in pH (from 7.4 to 7.75-7.85) significantly increased the protein binding of both OX and MO, underlining the necessity to conduct protein binding studies at physiological pH and temperature. The serum protein binding of both opioids was independent of drug concentration in the therapeutic range (5-100 ng/ml) but was dependent on the protein concentration. In serum containing albumin and AAG concentrations within the normal ranges, the binding of OX to albumin and AAG would be in the ranges 31-39% and 5-10%, respectively, and the binding of morphine would be 26-34% and 4-5%, respectively. (SAB)

L212 ANSWER 7 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN

ACCESSION NUMBER: 1993-52909 DRUGU P Full-text

TITLE: Determination of the Serum Protein Binding of Oxycodone and Morphine Using Ultrafiltration.

AUTHOR: Leow K P; Wright A M E; Cramond T; Smith M T

LOCATION: Brisbane, Australia

SOURCE: Ther. Drug Monit. (15, No. 5, 440-47, 1993) 6 Tab. 23 Ref.

CODEN: TDMODV ISSN: 0305-4356

AVAIL. OF DOC.: Department of Pharmacy, University of Queensland, Brisbane, Queensland 4072, Australia.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT; MPC

FILE SEGMENT: Literature

AN 1993-52909 DRUGU P Full-text

AB Serum protein binding of both oxycodone (OX) and morphine (MO) was fairly low and independent of drug concentration in the therapeutic range, but increased with increasing levels of total protein and of purified HSA or human alpha₁-acid glycoprotein (AAG, both Sigma-Chemical), in blood samples from healthy subjects. Albumin was the major binding protein for both OX and MO. Bound

10

of OC and at least 60 ug of NOC. A significantly shorter duration of antinociception occurred after OC than after M or NOC. i.c.v. administration of NAL markedly reduced the degree of antinociception produced by the subsequent i.c.v. administration of OC and NOC, indicating that the antinociceptive effects of OC and NOC are mediated by opioid receptors. A range of dose-dependent excitatory effects (allodynia, excessive facial grooming, tremor, Straub tail, myoclonic jerks, generalized seizures) were also observed in rats which received i.c.v. NOC, the severity of which was reduced but not eliminated by the subsequent administration of NAL (20 ug i.c.v.). (E54/RSV)

L212 ANSWER 9 OF 16 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN

ACCESSION NUMBER: 1994-06518 DRUGU P Full-text

TITLE: A New Metabolite of Oxycodone in Humans.

AUTHOR: Rose F B; Cramond T; Smith M T

CORPORATE SOURCE: Univ. Queensland

LOCATION: Brisbane, Australia

SOURCE: Clin. Exp. Pharmacol. Physiol. (Suppl. 1, 63, 1993) 1 Ref.

CODEN: CEXPB9 ISSN: 0305-1870

AVAIL. OF DOC.: Department of Pharmacy, University of Queensland, Qld 4072, Australia.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT; MPC

FILE SEGMENT: Literature

AN 1994-06518 DRUGU P Full-text

AB The metabolism of oxycodone (OC), a semi-synthetic opioid derivative with a reported efficacy approximately 0.7 that of morphine for the management of cancer pain, was studied in 8 cancer patients receiving OC chronically and in 5 healthy volunteers after a single p.o. dose. Urinary recovery of OC, noroxycodone (NOC) and oxymorphone (OM) was only 25%. However, an unstable metabolite was found, that accounted for at least 50% of the OC dose, and was thought to be a catechol derivative of OM. (congress abstract).

ABEX As OC has low affinity for mu-opioid receptor (K_d more than 1 uM), it is postulated that OC's analgesic efficacy may be due to formation of 1 or more active metabolites. The current studies both in cancer patients receiving OC chronically (40 mg daily) and in healthy volunteers after a single oral dose (10 mg) showed that the mean total urinary recovery of OC, NOC and OM (conjugated and unconjugated) was only 25%. Also, the OM urinary concentration (conjugated and unconjugated) was below the limits of detection (less than 0.5 ug/ml) in all urine samples. After incubation of OC urine with beta-glucuronidase, a new metabolite accounting for at least 50% of the OC dose, appeared in the HPLC chromatogram. In healthy volunteers this new metabolite only appeared in the 2nd 12 hr period after dosing. This putative OC metabolite was difficult to isolate because it is unstable both in unbuffered urine and in HPLC mobile phase. One possible structure for the putative new metabolite of OC which is consistent with the UV spectrum and with its instability in aqueous fluids is a catechol derivative of OM. (E54/RSV)

L212 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS ON STN DUPLICATE 1

ACCESSION NUMBER: 2005:219720 CAPLUS Full-text

DOCUMENT NUMBER: 142:274052

TITLE: Methods and compositions using sub-analgesic doses of a μ opioid agonist and oxycodone for reducing the risk associated with the administration of opioid analgesics in patients with diagnosed or undiagnosed respiratory illness

INVENTOR(S): Pace, Gary W.; Smith, Marce T.

PATENT ASSIGNER(S): USA

12

SOURCE: U.S. Pat. Appl. Publ., 11 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 200503659	A1	20050310	US 2003-661458	20030910
WO 2005025621	A1	20050324	WO 2004-US29731	20040910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GR, GM, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RU, SC, SD, SE, SG, SK, SL, SM, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MG, MW, NA, SD, SE, SI, SN, ST, SZ, TD, TG, TZ, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
SE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GT, GW, ML, MR, NE, SN, TD, TO				
EP 1667723	A1	20060614	EP 2004-783810	20040910
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRIORITY APPLN. INFO.: US 2003-661458 A1 20030910 WO 2004-US29731 W 20040910				

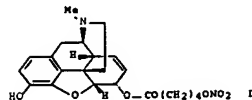
ED Entered STN: 11 Mar 2005
 AB The invention discloses methods for reducing the risk associated with the administration of opioid analgesics in patients diagnosed or undiagnosed with respiratory illness by administering an analgesic composition comprising a sub-analgesic dosage of a μ -opioid agonist selected from morphine, fentanyl, sufentanil, alfentanil, oxycodone and hydromorphone, or a pharmaceutically acceptable salt thereof, and a sub-analgesic dosage of oxycodone, which is a κ 2-opioid agonist, or a pharmaceutically acceptable salt thereof.

L212 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS ON STN DUPLICATE 3
 ACCESSION NUMBER: 2003:75712 CAPLUS Full-text
 DOCUMENT NUMBER: 139:271069
 TITLE: Methods and compositions including nitric oxide donors and opioid analgesics for pain relief
 INVENTOR(S): Smith, Maree Therese; Brown, Lindsey; Harvey, Mark Bradford Pullar; Williams, Craig McKenzie
 PATENT ASSIGNER(S): The University of Queensland, Australia
 SOURCE: PCT Int. Appl., 69 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078437	A1	20030925	WO 2003-AU335	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, GM, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT				

13

TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KO, KZ, MD, RU, TJ, TM, AT, BE, BG, BO, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GT, GW, ML, MR, NE, SN, TD, TO
 CA 2479098 A1 20030925 CA 2003-2479098 20030320
 AU 2003209850 A1 20030929 AU 2003-209850 20030320
 US 2003119494 A1 20031127 US 2003-393050 20030320
 EP 1495026 A1 20050112 EP 2003-744274 20030320
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK
 JP 200524676 T2 20050818 JP 2003-576442 20030320
 CN 1703416 A 20051130 CN 2003-095229 20030320
 PRIORITY APPLN. INFO.: US 2002-366594 P 20020320
 WO 2003-AU335 W 20030320
 OTHER SOURCE(S): MARPAT 139:271069
 ED Entered STN: 26 Sep 2003
 GI



AB Comps. and methods that induce, promote or otherwise facilitate pain relief are disclosed. These compps. and methods comprise a nitric oxide donor which either directly or indirectly prevents, attenuates or reverses the development of reduced opioid sensitivity, together with a compound which activates the opioid receptor that is the subject of the reduced opioid sensitivity. The compps. and methods prevent or alleviate pain, especially in neuropathic conditions and even more especially in peripheral neuropathic conditions such as painful diabetic neuropathy. The preferred nitric oxide donor is L-arginine, while the preferred compps. which activate the opioid receptor are morphine and oxycodone. Conjugate compps. comprising the nitric oxide donor and an opioid analgesic are also disclosed. Preparation of morphine-NO donor conjugates, e.g. 1, is also described.
 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L212 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS ON STN DUPLICATE 5
 ACCESSION NUMBER: 1997:361742 CAPLUS Full-text
 DOCUMENT NUMBER: 126:325531
 TITLE: Production of analgesic synergy by co-administration of sub-analgesic doses of a μ -opioid agonist and a κ 2-opioid agonist
 INVENTOR(S): Smith, Maree; Rosa, Fraser
 PATENT ASSIGNER(S): University of Queensland, Australia; Lynx Project Limited; Smith, Maree; Rosa, Fraser
 SOURCE: PCT Int. Appl., 83 pp.
 CODEN: PIXXD2

14

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714438	A1	19970424	WO 1996-AU656	19961021
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SP, BJ, CF, CG				
ZA 9608808	A	19970527	ZA 1996-8808	19961019
CA 2235375	AA	19970424	CA 1996-2235375	19961021
AU 9672076	A1	19970507	AU 1996-72076	19961021
AU 966691	B2	19960624		
EP 871488	A1	19961021	EP 1996-933277	19961021
EP 871488	B1	20050413		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1204264	A	19990106	CN 1996-199071	19961021
CN 1104910	B	20030409		
AT 292982	E	20050415	AT 1996-933277	19961021
ES 2241003	T3	20051016	ES 1996-933277	19961021
US 6310072	B1	20011030	US 1997-921187	19970829
PRIORITY APPLN. INFO.: AU 1995-6038 A 19951019 WO 1996-AU656 W 19961021				

ED Entered STN: 11 Jun 1997
 AB An analgesic composition comprises a sub-analgesic dosage of a μ -opioid agonist or analog or derivative or pharmaceutically acceptable salts thereof and a sub-analgesic dosage of a κ 2-opioid agonist or analog or derivative or pharmaceutically acceptable salts thereof. The μ -opioid agonist may be morphine, fentanyl, sufentanil, alfentanil, or hydromorphone; the κ 2-opioid agonist may be oxycodone.

L212 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2006 ACS ON STN
 ACCESSION NUMBER: 2003:757520 CAPLUS Full-text
 DOCUMENT NUMBER: 139:255380
 TITLE: Method of treatment and prophylaxis of neuropathic condition
 INVENTOR(S): Smith, Maree Therese; Brown, Lindsey
 PATENT ASSIGNER(S): The University of Queensland, Australia
 SOURCE: PCT Int. Appl., 87 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003077912	A1	20030925	WO 2003-AU336	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, GM, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM				

15

PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KO, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GT, GW, ML, MR, NE, SN, TD, TO
 AU 2003209851 A1 20030929 AU 2003-209851 20030320
 US 2003199424 A1 20031023 US 2003-393056 20030320
 PRIORITY APPLN. INFO.: US 2002-365858 P 20020320
 WO 2003-AU336 W 20030320

ED Entered STN: 26 Sep 2003
 AB The invention is involves the use of angiotensin II receptor 1 (AT1 receptor) antagonists for the treatment, prophylaxis, reversal and/or symptomatic relief of a neuropathic condition, especially a peripheral neuropathic condition such as painful diabetic neuropathy, in vertebrate animals and particularly in human subjects. The invention also discloses the use of AT1 receptor antagonists for preventing, attenuating or reversing the development of reduced opioid sensitivity, and more particularly reduced opioid analgesic sensitivity, in individuals and especially in individuals having, or at risk of developing, a neuropathic condition.
 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L212 ANSWER 14 OF 16 WPX COPYRIGHT 2006 THE THOMSON CORP ON STN
 ACCESSION NUMBER: 2006-464147 [47] WPX
 DOC. NO. CFI: C2006-145568 [47]
 TITLE: Method of producing analgesia, useful to relieve pain e.g. moderate to severe cancer pain and post surgical pain, comprises administering a nitric oxide donor and an opioid analgesic
 INVENTOR: SMITH M T
 PATENT ASSIGNER: (UYUQ-C) UNIV QUEENSLAND
 COUNTRY COUNT: 111
 PATENT INFO ABBR.: B02

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 200606362	A1	20060629	(200647)	EN	87	[11]

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 200606362	A1	WO 2005-AU1976	20051223

PRIORITY APPLN. INFO: AU 2004-907352 20041224

ED 20060724
 AN 2006-464147 [47] WPX
 AB WO 200606362 A1 UPAB: 20060724

NOVELTY - Method of producing analgesia (A) in a subject comprises administering a nitric oxide donor (II) and an opioid analgesic, where (II) delivers nitric oxide (II) at a rate of 0.0002-2 nmol/kg/hour.
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for new compounds of formula (I).
 ACTIVITY - Analgesic.
 MECHANISM OF ACTION - None given.
 USE - (A) is useful to relieve pain (moderate to severe cancer pain, moderate to severe post surgical pain, pain following physical trauma, pain associated

16

with cardiac infarction and inflammatory pain) (claimed). No biological data given.
 ADVANTAGE - (A) enhances the endogenous production of nitroethiols and reduces the endogenous production of peroxynitrite.

L212 ANSWER 15 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005175148 EMBASE Full-text
 TITLE: Co-administration of oxycodone and morphine and analgesic synergy re-examined [1] (multiple letters).
 AUTHOR: Smith M.T.; De La Iglesia F.A.; Grath M.; Massalha W.; Pud D.; Adler R.; Eisenberg R.
 CORPORATE SOURCE: F.A. De La Iglesia, University of Michigan, Medical School, Ann Arbor, MI, Australia. delaisgf@umich.edu
 SOURCE: British Journal of Clinical Pharmacology, (2005) Vol. 59, No. 4, pp. 486-488.
 ISBN: 0306-5551 CODEN: BCPHEM
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Letter
 FILE SEGMENT: 008 Neurology and Neurosurgery
 037 Drug Literature Index
 LANGUAGE: English
 ENTRY DATE: Entered STN: 12 May 2005
 Last Updated on STN: 12 May 2005
 ED Entered STN: 12 May 2005
 Last Updated on STN: 12 May 2005
 DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L212 ANSWER 16 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 97021905 EMBASE Full-text
 DOCUMENT NUMBER: 1997021905
 TITLE: HIV-1 protease inhibitors: A review for clinicians.
 AUTHOR: Deeks S.G.; Smith M.; Holodny M.; Kahn J.O.
 CORPORATE SOURCE: Dr. J.O. Kahn, University of California, San Francisco General Hospital, 995 Potrero Ave, San Francisco, CA 94110, United States. jkahn@sfids.ucsf.edu
 SOURCE: Journal of the American Medical Association, (1997) Vol. 277, No. 2, pp. 145-153.
 Refs: 59
 ISSN: 0098-7484 CODEN: JAMAAP
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 006 Internal Medicine
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 15 Feb 1997
 Last Updated on STN: 15 Feb 1997
 ED Entered STN: 15 Feb 1997
 Last Updated on STN: 15 Feb 1997

AB Objective: The clinical care of people infected with human immunodeficiency virus (HIV) has been substantially affected by the introduction of HIV-specific protease inhibitors (PIs). The 4 PIs available are zidovudine, zalcitabine, didanosine, and zalcitabine. Comparison studies have not been reported; therefore, an assessment of the available data to aid clinicians and patients in choosing appropriate treatment will be

17

presented. Data Sources: A systematic review of peer-reviewed publications, abstracts from national and international conferences, and product registration information through September 1996. Study Selection and Data Extraction: Criteria used to select studies include their relevance to PIs, having been published in the English language, and pertinence for clinicians. Data quality and validity included the venue of the publication and relevance to clinical care. Data Synthesis: Oral administration of zidovudine, didanosine, or zalcitabine generates sustainable drug serum levels to effectively inhibit the protease enzyme; however, zalcitabine may not generate sustained levels necessary to inhibit the protease enzyme. Patients treated with zidovudine, didanosine, or zalcitabine experience similar reductions in viral load and increases in CD4+ lymphocytes; smaller effects occur among those treated with zalcitabine. Two randomized placebo-controlled studies demonstrated among patients with severe immune system suppression and substantial zidovudine treatment experience demonstrated reduced HIV disease progression and reduced mortality with PI treatment. Genotypic resistance to PIs occurs; the clinical relevance of resistance is unclear. The costs of these agents including required monitoring impose new and substantial costs. Conclusions: The PIs have emerged as critical drugs for people with HIV infection. Optimal use involves combination with reverse transcriptase inhibitors. Resistance develops to each agent, and cross-resistance is likely. These agents must be used at full doses with attention to ensuring patient compliance. The expense of these agents may be offset by forestalling disease progression and death and returning people to productive life. Selecting the initial PI must be individualized, and factors to consider include proven activity, possible toxicities, dosing regimens, drug interactions, and costs.

18

TEXT SEARCH

=> fil capl; d que 141; d que 144
 FILE 'CAPLUS' ENTERED AT 11:12:31 ON 14 DEC 2006
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 14 Dec 2006 VOL 145 ISS 25
 FILE LAST UPDATED: 13 Dec 2006 (20061213/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.csa.org/infopolicy.html>
 'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L5 1 SEA FILE-REGISTRY ABB-ON MORPHINE/CN
 L6 1 SEA FILE-REGISTRY ABB-ON FENTANYL/CN
 L7 1 SEA FILE-REGISTRY ABB-ON SUFENTANYL/CN
 L8 1 SEA FILE-REGISTRY ABB-ON ALFENTANYL/CN
 L9 1 SEA FILE-REGISTRY ABB-ON OXYMORPHONE/CN
 L10 1 SEA FILE-REGISTRY ABB-ON HYDROMORPHONE/CN
 L11 1 SEA FILE-REGISTRY ABB-ON OXYCODONE/CN
 L12 31087 SEA FILE-CAPLUS ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)
 L13 1073 SEA FILE-CAPLUS ABB-ON L11
 L14 12914 SEA FILE-CAPLUS ABB-ON OPIOIDS/CT
 L15 1209 SEA FILE-CAPLUS ABB-ON L14(L) KAPPA/OBI
 L16 1944 SEA FILE-CAPLUS ABB-ON L14(L) MU/OBI
 L17 56591 SEA FILE-CAPLUS ABB-ON AGONISTS/OBI
 L18 368 SEA FILE-CAPLUS ABB-ON L15(L) L17
 L19 454 SEA FILE-CAPLUS ABB-ON L16(L) L17
 L20 19117 SEA FILE-CAPLUS ABB-ON RESPIRATORY TRACT/OBI
 L21 76 SEA FILE-CAPLUS ABB-ON L20(L) CARCINOMA/OBI
 L22 25232 SEA FILE-CAPLUS ABB-ON ASTHMA/OBI
 L23 424 SEA FILE-CAPLUS ABB-ON BRONCHITIS/OBI OR BRONCHI?/OBI (L) DI
 LATATION/OBI OR KARTAGNER/OBI
 L24 28786 SEA FILE-CAPLUS ABB-ON TUBERCULOSIS/OBI
 L25 4089 SEA FILE-CAPLUS ABB-ON BRONCHITIS/OBI
 L26 120 SEA FILE-CAPLUS ABB-ON RESPIRATORY SYSTEM, NEOPLASM/CT
 L27 35540 SEA FILE-CAPLUS ABB-ON LUNG, NEOPLASM/CT
 L28 4982 SEA FILE-CAPLUS ABB-ON CHRONIC OBSTRUCTIVE PULMONARY/OBI OR
 COPD/OBI
 L29 7726 SEA FILE-CAPLUS ABB-ON BRONCHOPNEUMONIA/OBI OR PNEUMONIA/OBI
 L30 136 SEA FILE-CAPLUS ABB-ON LARYNGITIS/OBI
 L31 1101 SEA FILE-CAPLUS ABB-ON SINUSITIS/OBI
 L32 2601 SEA FILE-CAPLUS ABB-ON EMPHYSEMA/OBI
 L33 6378 SEA FILE-CAPLUS ABB-ON FIBROSINO/OBI (L) ALVEOLITIS/OBI OR

(PULMONARY/OBI OR LUNG/OBI OR RESPIRATORY/OBI) (L) (FIBROSIS/OBI
 OR SARCOIDOSIS/OBI)
 L34 6 SEA FILE-CAPLUS ABB-ON SLEEP DISORDERS/CT (L) RESPIRATORY/OBI
 L35 943 SEA FILE-CAPLUS ABB-ON SLEEP/OBI (L) APNEA/OBI
 L36 1691 SEA FILE-CAPLUS ABB-ON SARCOIDOSIS/CT
 L37 39125 SEA FILE-CAPLUS ABB-ON DRUG INTERACTIONS-OLD, NT/CT
 L38 4450 SEA FILE-CAPLUS ABB-ON DRUG DELIVERY SYSTEMS-OLD/CT (L) COMB?/OB
 I
 L39 16989 SEA FILE-CAPLUS ABB-ON COMBINATION CHEMOTHERAPY/CT
 L40 5480 SEA FILE-CAPLUS ABB-ON COMB?/OBI (L) PHARMAC?/OBI
 L41 6 SEA FILE-CAPLUS ABB-ON (L12 OR L19) AND (L13 OR L18) AND (L21
 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30
 OR L31 OR L32 OR L33 OR L34 OR L35 OR L36) AND (L37 OR L38 OR
 L39 OR L40)
 L5 1 SEA FILE-REGISTRY ABB-ON MORPHINE/CN
 L6 1 SEA FILE-REGISTRY ABB-ON FENTANYL/CN
 L7 1 SEA FILE-REGISTRY ABB-ON SUFENTANYL/CN
 L8 1 SEA FILE-REGISTRY ABB-ON ALFENTANYL/CN
 L9 1 SEA FILE-REGISTRY ABB-ON OXYMORPHONE/CN
 L10 1 SEA FILE-REGISTRY ABB-ON HYDROMORPHONE/CN
 L11 1 SEA FILE-REGISTRY ABB-ON OXYCODONE/CN
 L12 31087 SEA FILE-CAPLUS ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)
 L13 1073 SEA FILE-CAPLUS ABB-ON L11
 L14 12914 SEA FILE-CAPLUS ABB-ON OPIOIDS/CT
 L15 1209 SEA FILE-CAPLUS ABB-ON L14(L) KAPPA/OBI
 L16 1944 SEA FILE-CAPLUS ABB-ON L14(L) MU/OBI
 L17 56591 SEA FILE-CAPLUS ABB-ON AGONISTS/OBI
 L18 368 SEA FILE-CAPLUS ABB-ON L15(L) L17
 L19 454 SEA FILE-CAPLUS ABB-ON L16(L) L17
 L20 19117 SEA FILE-CAPLUS ABB-ON RESPIRATORY TRACT/OBI
 L21 76 SEA FILE-CAPLUS ABB-ON L20(L) CARCINOMA/OBI
 L22 25232 SEA FILE-CAPLUS ABB-ON ASTHMA/OBI
 L23 424 SEA FILE-CAPLUS ABB-ON BRONCHITIS/OBI OR BRONCHI?/OBI (L) DI
 LATATION/OBI OR KARTAGNER/OBI
 L24 28786 SEA FILE-CAPLUS ABB-ON TUBERCULOSIS/OBI
 L25 4089 SEA FILE-CAPLUS ABB-ON BRONCHITIS/OBI
 L26 120 SEA FILE-CAPLUS ABB-ON RESPIRATORY SYSTEM, NEOPLASM/CT
 L27 35540 SEA FILE-CAPLUS ABB-ON LUNG, NEOPLASM/CT
 L28 4982 SEA FILE-CAPLUS ABB-ON CHRONIC OBSTRUCTIVE PULMONARY/OBI OR
 COPD/OBI
 L29 7726 SEA FILE-CAPLUS ABB-ON BRONCHOPNEUMONIA/OBI OR PNEUMONIA/OBI
 L30 136 SEA FILE-CAPLUS ABB-ON LARYNGITIS/OBI
 L31 1101 SEA FILE-CAPLUS ABB-ON SINUSITIS/OBI
 L32 2601 SEA FILE-CAPLUS ABB-ON EMPHYSEMA/OBI
 L33 6378 SEA FILE-CAPLUS ABB-ON FIBROSINO/OBI (L) ALVEOLITIS/OBI OR
 (PULMONARY/OBI OR LUNG/OBI OR RESPIRATORY/OBI) (L) (FIBROSIS/OBI
 OR SARCOIDOSIS/OBI)
 L34 6 SEA FILE-CAPLUS ABB-ON SLEEP DISORDERS/CT (L) RESPIRATORY/OBI
 L35 943 SEA FILE-CAPLUS ABB-ON SLEEP/OBI (L) APNEA/OBI
 L36 1691 SEA FILE-CAPLUS ABB-ON SARCOIDOSIS/CT
 L42 552 SEA FILE-CAPLUS ABB-ON (L12 OR L19) (L) (COMB?/OBI OR COADMIN?/O
 BI OR CODRUGS/OBI OR CONCOMITANT?/OBI OR CONCURRENT?/OBI OR
 BLEND?/OBI OR MIXTURES/OBI)
 L43 82 SEA FILE-CAPLUS ABB-ON (L13 OR L18) (L) (COMB?/OBI OR COADMIN?/O
 BI OR CODRUGS/OBI OR CONCOMITANT?/OBI OR CONCURRENT?/OBI OR
 BLEND?/OBI OR MIXTURES/OBI)
 L44 3 SEA FILE-CAPLUS ABB-ON L42 AND L43 AND (L21 OR L32 OR L23 OR

19

20

L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR
L33 OR L34 OR L35 OR L36)

>> # 141,144 not 1210

L213 5 (L41 OR L44) NOT L210

>> fil embase; d que 182; d que 184

FILE 'EMBASE' ENTERED AT 11:12:33 ON 14 DEC 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE COVERS 1974 TO 13 DEC 2006 (20061213/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default)
and biweekly.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

L48 53452 SEA FILE-EMBASE ABB-ON MORPHINE/CT
L49 26736 SEA FILE-EMBASE ABB-ON FENTANYL/CT OR FENTANYL CITRATE/CT
L50 4395 SEA FILE-EMBASE ABB-ON SUFENTANIL/CT OR SUFENTANIL CITRATE/CT

L51 4482 SEA FILE-EMBASE ABB-ON ALFENTANIL/CT
L52 805 SEA FILE-EMBASE ABB-ON OXYMORPHONE/CT
L53 2957 SEA FILE-EMBASE ABB-ON HYDROMORPHONE/CT
L54 3754 SEA FILE-EMBASE ABB-ON OXYCODONE/CT
L55 84233 SEA FILE-EMBASE ABB-ON ASTHMA-NT/CT
L56 4535 SEA FILE-EMBASE ABB-ON BRONCHIECTASIS-NT/CT
L57 15140 SEA FILE-EMBASE ABB-ON LUNG TUBERCULOSIS/CT
L58 26377 SEA FILE-EMBASE ABB-ON CHRONIC OBSTRUCTIVE LUNG DISEASE/CT
L59 22047 SEA FILE-EMBASE ABB-ON BRONCHITIS-NT/CT
L60 2275 SEA FILE-EMBASE ABB-ON BRONCHOPNEUMONIA/CT
L61 2500 SEA FILE-EMBASE ABB-ON LARYNGITIS-NT/CT
L62 12991 SEA FILE-EMBASE ABB-ON SINUSITIS-NT/CT
L63 13249 SEA FILE-EMBASE ABB-ON EMPHYSEMA-NT/CT
L64 2738 SEA FILE-EMBASE ABB-ON FIBROSING ALVEOLITIS/CT
L65 19527 SEA FILE-EMBASE ABB-ON LUNG FIBROSIS-NT/CT
L66 11397 SEA FILE-EMBASE ABB-ON SARCOIDOSIS/CT
L67 91685 SEA FILE-EMBASE ABB-ON LUNG CANCER-NT/CT
L68 11977 SEA FILE-EMBASE ABB-ON SLEEP APNEA SYNDROME/CT
L75 38068 SEA FILE-EMBASE ABB-ON DRUG POTENTIATION/CT
L76 12328 SEA FILE-EMBASE ABB-ON MU OPIATE RECEPTOR AGONIST/CT
L77 945 SEA FILE-EMBASE ABB-ON KAPPA OPIATE RECEPTOR AGONIST/CT
L78 0 SEA FILE-EMBASE ABB-ON (L48 OR L49 OR L50 OR L51 OR L52 OR
L53 OR L76) AND (L77 OR L54) AND L75 AND (L55 OR L56 OR L57 OR
L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR L66 OR
L67 OR L68)

L48 53452 SEA FILE-EMBASE ABB-ON MORPHINE/CT
L49 26736 SEA FILE-EMBASE ABB-ON FENTANYL/CT OR FENTANYL CITRATE/CT
L50 4395 SEA FILE-EMBASE ABB-ON SUFENTANIL/CT OR SUFENTANIL CITRATE/CT

L51 4482 SEA FILE-EMBASE ABB-ON ALFENTANIL/CT
L52 805 SEA FILE-EMBASE ABB-ON OXYMORPHONE/CT

21

L53 2957 SEA FILE-EMBASE ABB-ON HYDROMORPHONE/CT
L54 3754 SEA FILE-EMBASE ABB-ON OXYCODONE/CT
L55 84233 SEA FILE-EMBASE ABB-ON ASTHMA-NT/CT
L56 4535 SEA FILE-EMBASE ABB-ON BRONCHIECTASIS-NT/CT
L57 15140 SEA FILE-EMBASE ABB-ON LUNG TUBERCULOSIS/CT
L58 26377 SEA FILE-EMBASE ABB-ON CHRONIC OBSTRUCTIVE LUNG DISEASE/CT
L59 22047 SEA FILE-EMBASE ABB-ON BRONCHITIS-NT/CT
L60 2275 SEA FILE-EMBASE ABB-ON BRONCHOPNEUMONIA/CT
L61 2500 SEA FILE-EMBASE ABB-ON LARYNGITIS-NT/CT
L62 12991 SEA FILE-EMBASE ABB-ON SINUSITIS-NT/CT
L63 13249 SEA FILE-EMBASE ABB-ON EMPHYSEMA-NT/CT
L64 2738 SEA FILE-EMBASE ABB-ON FIBROSING ALVEOLITIS/CT
L65 19527 SEA FILE-EMBASE ABB-ON LUNG FIBROSIS-NT/CT
L66 11397 SEA FILE-EMBASE ABB-ON SARCOIDOSIS/CT
L67 91685 SEA FILE-EMBASE ABB-ON LUNG CANCER-NT/CT
L68 11977 SEA FILE-EMBASE ABB-ON SLEEP APNEA SYNDROME/CT
L69 493 SEA FILE-EMBASE ABB-ON L54(L) (CB OR IT)/CT CB-DRUG COMBINATIONS
L76 1238 SEA FILE-EMBASE ABB-ON MU OPIATE RECEPTOR AGONIST/CT
L77 945 SEA FILE-EMBASE ABB-ON KAPPA OPIATE RECEPTOR AGONIST/CT
L78 208 SEA FILE-EMBASE ABB-ON L76(L) (CB OR IT)/CT IT-DRUG INTERACTIONS
L79 145 SEA FILE-EMBASE ABB-ON L77(L) (CB OR IT)/CT
L80 10397 SEA FILE-EMBASE ABB-ON L53(L) (L) (CB OR IT)/CT
L84 2 SEA FILE-EMBASE ABB-ON (L72 OR L79) AND (L80 OR L78) AND (L55
OR L56 OR L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64
OR L65 OR L66 OR L67 OR L68)

>> # 184 not 181

L214 2 L84 NOT L81

>> fil drugu; d que 1107

FILE 'DRUGU' ENTERED AT 11:12:35 ON 14 DEC 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE LAST UPDATED: 11 DEC 2006 <20061211/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

L5 1 SEA FILE-REGISTRY ABB-ON MORPHINE/CN
L6 1 SEA FILE-REGISTRY ABB-ON FENTANYL/CN
L7 1 SEA FILE-REGISTRY ABB-ON SUFENTANIL/CN
L8 1 SEA FILE-REGISTRY ABB-ON ALFENTANIL/CN
L9 1 SEA FILE-REGISTRY ABB-ON OXYMORPHONE/CN
L10 1 SEA FILE-REGISTRY ABB-ON HYDROMORPHONE/CN
L11 1 SEA FILE-REGISTRY ABB-ON OXYCODONE/CN
L17 9457 SEA FILE-DRUGU ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)
L88 269 SEA FILE-DRUGU ABB-ON L11
L89 19705 SEA FILE-DRUGU ABB-ON MORPHINE/CT
L90 11240 SEA FILE-DRUGU ABB-ON FENTANYL/CT
L91 2280 SEA FILE-DRUGU ABB-ON SUFENTANIL/CT
L92 2680 SEA FILE-DRUGU ABB-ON ALFENTANIL/CT
L93 252 SEA FILE-DRUGU ABB-ON OXYMORPHONE/CT
L94 866 SEA FILE-DRUGU ABB-ON HYDROMORPHONE/CT

22

L95 966 SEA FILE-DRUGU ABB-ON OXYCODONE/CT
L97 125676 SEA FILE-DRUGU ABB-ON COMB/CT
L98 41301 SEA FILE-DRUGU ABB-ON DRUG INTERACTIONS/CC
L100 31287 SEA FILE-DRUGU ABB-ON ASTHMA OR BRONCHIECTASIS OR BRONCHI? (2A)
DILATATION OR KARTAGENER OR TUBERCULOSIS
L101 3808 SEA FILE-DRUGU ABB-ON COPD OR CHRONIC OBSTRUCTIVE (M) (LUNG OR
PULMONARY OR RESPIRATORY)
L102 24212 SEA FILE-DRUGU ABB-ON BRONCHITIS OR BRONCHOPNEUMONIA OR
PNEUMONIA OR LARYNGITIS OR SINUSITIS OR EMPHYSEMA
L103 1971 SEA FILE-DRUGU ABB-ON FIBROSING ALVEOLITIS OR FIBROSIS (A) (LUNG
OR PULMONARY OR RESPIRATORY)
L104 951 SEA FILE-DRUGU ABB-ON SARCOIDOSIS
L105 17785 SEA FILE-DRUGU ABB-ON (LUNG OR PULMONARY OR RESPIRATORY) (2A) (C
ANCERS OR NEOPLAS? OR CARCINOMAS)
L106 433 SEA FILE-DRUGU ABB-ON SLEEP APNEA
L107 4 SEA FILE-DRUGU ABB-ON ((L97 OR L98) AND (L87 OR L89 OR L90 OR
L91 OR L92 OR L93 OR L94) AND (L88 OR L95)) AND (L100 OR L101
OR L102 OR L103 OR L104 OR L105 OR L106)

>> # 1107 not 196

L215 4 L107 NOT L96

>> fil wpi; d que 1134; d que 1142

FILE 'WPIX' ENTERED AT 11:12:38 ON 14 DEC 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE LAST UPDATED: 8 DEC 2006 <20061208/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200679 <200679/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training-center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
<http://scientific.thomson.com/media/scpd/ipcdwpi.pdf>

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<
'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

L117 198 SEA FILE-WPIX ABB-ON MU OPIOIDS/BI, ABEX
L118 186 SEA FILE-WPIX ABB-ON KAPPA/BI, ABEX (1M) OPIOIDS/BI, ABEX
L119 12146 SEA FILE-WPIX ABB-ON B14-L01/MC OR C14-L01/MC -AGONISTS
L120 100 SEA FILE-WPIX ABB-ON L117(2A)AGONISTS/BI, ABEX OR L117 AND
L119)
L121 102 SEA FILE-WPIX ABB-ON L118(2A)AGONISTS/BI, ABEX OR (L118 AND
L119)
L122 486502 SEA FILE-WPIX ABB-ON (M782 OR P867)/M0, M1, M2, M3, M4, M5, M6 OR
A61K045/IPC OR (B12-C09 OR C12-C09 OR B14-S09 OR C14-S09)/MC
L124 28604 SEA FILE-WPIX ABB-ON ASTHMA/BI, ABEX OR BRONCHIECTASIS/BI, ABEX
OR BRONCHI?/BI, ABEX (2A) DILATATION/BI, ABEX OR KARTAGENER/BI, ABEX
OR TUBERCULOSIS/BI, ABEX
L125 5007 SEA FILE-WPIX ABB-ON COPD/BI, ABEX OR CHRONIC OBSTRUCTIVE/BI, AB
EX (M) (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR RESPIRATORY/BI, ABEX)
L126 11360 SEA FILE-WPIX ABB-ON BRONCHITIS/BI, ABEX OR BRONCHOPNEUMONIA/BI
ABEX OR PNEUMONIA/BI, ABEX OR LARYNGITIS/BI, ABEX OR SINUSITIS/B
I, ABEX OR EMPHYSEMA/BI, ABEX
L127 2462 SEA FILE-WPIX ABB-ON FIBROSING ALVEOLITIS/BI, ABEX OR FIBROSIS/
BI, ABEX (A) (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR RESPIRATORY/BI, AB
EX)
L128 3624 SEA FILE-WPIX ABB-ON SARCOIDOSIS/BI, ABEX OR SLEEP APNEA/BI, AB
EX
L129 8806 SEA FILE-WPIX ABB-ON (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR FIBROSIS/
OR RESPIRATORY/BI, ABEX) (2A) (CANCER/BI, ABEX OR NEOPLAS?/BI, ABEX
OR CARCINOMA/BI, ABEX)
L134 1 SEA FILE-WPIX ABB-ON L120 AND L121 AND L122 AND (L124 OR L125
OR L126 OR L127 OR L128 OR L129)

L111 3147 SEA FILE-WPIX ABB-ON MORPHINE/BI, ABEX OR FENTANYL/BI, ABEX OR
ALFENTANIL/BI, ABEX OR SUFENTANIL/BI, ABEX OR OXYMORPHONE/BI, ABEX
OR MRZ2593/BI, ABEX OR MRZ 2593/BI, ABEX OR HYDROMORPHONE/BI, ABEX
X
L116 513 SEA FILE-WPIX ABB-ON OXYCODONE/BI, ABEX
L117 198 SEA FILE-WPIX ABB-ON MU OPIOIDS/BI, ABEX
L118 186 SEA FILE-WPIX ABB-ON KAPPA/BI, ABEX (1M) OPIOIDS/BI, ABEX
L124 28604 SEA FILE-WPIX ABB-ON ASTHMA/BI, ABEX OR BRONCHIECTASIS/BI, ABEX
OR BRONCHI?/BI, ABEX (2A) DILATATION/BI, ABEX OR KARTAGENER/BI, ABEX
OR TUBERCULOSIS/BI, ABEX
L125 5007 SEA FILE-WPIX ABB-ON COPD/BI, ABEX OR CHRONIC OBSTRUCTIVE/BI, AB
EX (M) (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR RESPIRATORY/BI, ABEX)
L126 11360 SEA FILE-WPIX ABB-ON BRONCHITIS/BI, ABEX OR BRONCHOPNEUMONIA/BI
ABEX OR PNEUMONIA/BI, ABEX OR LARYNGITIS/BI, ABEX OR SINUSITIS/B
I, ABEX OR EMPHYSEMA/BI, ABEX
L127 2462 SEA FILE-WPIX ABB-ON FIBROSING ALVEOLITIS/BI, ABEX OR FIBROSIS/
BI, ABEX (A) (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR RESPIRATORY/BI, AB
EX)
L128 3624 SEA FILE-WPIX ABB-ON SARCOIDOSIS/BI, ABEX OR SLEEP APNEA/BI, AB
EX
L129 8806 SEA FILE-WPIX ABB-ON (LUNG/BI, ABEX OR PULMONARY/BI, ABEX OR FIBROSIS/
OR RESPIRATORY/BI, ABEX) (2A) (CANCER/BI, ABEX OR NEOPLAS?/BI, ABEX
OR CARCINOMA/BI, ABEX)
L138 84 SEA FILE-WPIX ABB-ON L118(2A)AGONISTS/BI, ABEX
L139 61 SEA FILE-WPIX ABB-ON L117(2A)AGONISTS/BI, ABEX
L140 384 SEA FILE-WPIX ABB-ON ((L111 OR L139)) (5A) ((L116 OR L138))
L141 10 SEA FILE-WPIX ABB-ON L140(5A) (COMB?/BI, ABEX OR CODRU?/BI, ABEX

OR COADMIN?/BI.ABEX OR COADMIN?/BI.ABEX OR CONCURRENT?/BI.ABEX
OR BLEND?/BI.ABEX OR MIX?/BI.ABEX
L142 2 SEA FILE=WPX ABB=ON L141 AND (L124 OR L125 OR L126 OR L127
OR L128 OR L129)

=> s 1134,1142 not 1211

L216 2 (L134 OR L142) NOT L211

=> fil medl; d que 1189; d que 1197; d que 1207; d que 1179

FILE 'MEDLINE' ENTERED AT 11:12:43 ON 14 DEC 2006

FILE LAST UPDATED: 13 Dec 2006 (20061213/UP). FILE COVERS 1950 TO DATE.

In preparation for the annual MEDLINE reload, the National Library of Medicine (NLM) has suspended delivery of regular updates as of November 15, 2006. In-process and in-data-review records will resume delivery on November 21, 2006, and will continue to be added to MEDLINE until December 17, 2006.

On December 17, 2006, all regular MEDLINE updates from November 15 to December 16 will be added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R)) and 2007 tree numbers.

The annual reload will be available in early 2007.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L180(28104)SEA FILE=MEDLINE ABB=ON MORPHINE/CT
L181(10382)SEA FILE=MEDLINE ABB=ON FENTANYL-NT/CT
L182(294)SEA FILE=MEDLINE ABB=ON OXYMORPHONE/CT
L183(704)SEA FILE=MEDLINE ABB=ON HYDROMORPHONE/CT
L184(540)SEA FILE=MEDLINE ABB=ON OXYCODONE/CT
L185(108974)SEA FILE=MEDLINE ABB=ON DRUG INTERACTIONS-NT/CT
L186(42787)SEA FILE=MEDLINE ABB=ON DRUG COMBINATIONS/CT
L187(97253)SEA FILE=MEDLINE ABB=ON DRUG THERAPY, COMBINATION/CT
L188(15)SEA FILE=MEDLINE ABB=ON (L180 OR L181 OR L182 OR L183) AND
L184 AND (L185 OR L186 OR L187)
L189 3 SEA FILE=MEDLINE ABB=ON L188 AND SYNERG?

L190(108974)SEA FILE=MEDLINE ABB=ON DRUG INTERACTIONS-NT/CT
L191(42787)SEA FILE=MEDLINE ABB=ON DRUG COMBINATIONS/CT
L192(97253)SEA FILE=MEDLINE ABB=ON DRUG THERAPY, COMBINATION/CT
L193(1136)SEA FILE=MEDLINE ABB=ON RECEPTORS, OPIOID, MU/CT(L)AG/CT
L194(881)SEA FILE=MEDLINE ABB=ON RECEPTORS, OPIOID, KAPPA/CT(L)AG/CT
L195(23)SEA FILE=MEDLINE ABB=ON L193 AND L194 AND (L190 OR L191 OR
L192)
L196(240557)SEA FILE=MEDLINE ABB=ON DOSE-RESPONSE RELATIONSHIP, DRUG/CT
L197 1 SEA FILE=MEDLINE ABB=ON L195 AND L196 AND CONDITIONING,
OPERANT/CT

L198(28104)SEA FILE=MEDLINE ABB=ON MORPHINE/CT
L199(10382)SEA FILE=MEDLINE ABB=ON FENTANYL-NT/CT
L200(294)SEA FILE=MEDLINE ABB=ON OXYMORPHONE/CT
L201(704)SEA FILE=MEDLINE ABB=ON HYDROMORPHONE/CT
L202(540)SEA FILE=MEDLINE ABB=ON OXYCODONE/CT
L203(1136)SEA FILE=MEDLINE ABB=ON RECEPTORS, OPIOID, MU/CT(L)AG/CT
L204(881)SEA FILE=MEDLINE ABB=ON RECEPTORS, OPIOID, KAPPA/CT(L)AG/CT
L205(488)SEA FILE=MEDLINE ABB=ON (L198 OR L199 OR L200 OR L201 OR
L203) AND (L202 OR L204)
L206(8267)SEA FILE=MEDLINE ABB=ON COUGH/CT
L207 1 SEA FILE=MEDLINE ABB=ON L205 AND L206

L164(28104)SEA FILE=MEDLINE ABB=ON MORPHINE/CT
L165(10382)SEA FILE=MEDLINE ABB=ON FENTANYL-NT/CT
L166(294)SEA FILE=MEDLINE ABB=ON OXYMORPHONE/CT
L167(704)SEA FILE=MEDLINE ABB=ON HYDROMORPHONE/CT
L168(540)SEA FILE=MEDLINE ABB=ON OXYCODONE/CT
L169(124991)SEA FILE=MEDLINE ABB=ON LUNG DISEASES, OBSTRUCTIVE-NT/CT
L170(5936)SEA FILE=MEDLINE ABB=ON BRONCHITIS-NT/CT
L171(57086)SEA FILE=MEDLINE ABB=ON TUBERCULOSIS, PULMONARY-NT/CT
L172(3460)SEA FILE=MEDLINE ABB=ON BRONCHOPNEUMONIA/CT
L173(3610)SEA FILE=MEDLINE ABB=ON LARYNGITIS-NT/CT
L174(11628)SEA FILE=MEDLINE ABB=ON SINUSITIS-NT/CT
L175(13172)SEA FILE=MEDLINE ABB=ON PULMONARY FIBROSIS/CT
L176(1561)SEA FILE=MEDLINE ABB=ON SARCOIDOSIS, PULMONARY/CT
L177(113814)SEA FILE=MEDLINE ABB=ON LUNG NEOPLASMS-NT/CT
L178(12706)SEA FILE=MEDLINE ABB=ON SLEEP APNEA SYNDROMES-NT/CT
L179 1 SEA FILE=MEDLINE ABB=ON (L164 OR L165 OR L166 OR L167) AND
L168 AND (L169 OR L170 OR L171 OR L172 OR L173 OR L174 OR L175
OR L176 OR L177 OR L178)

=> s 1189,1197,1207,1179

L217 6 (L189 OR L197 OR L207 OR L179)

=> s dup rem 1217,1215,1213,1216,1214

FILE 'MEDLINE' ENTERED AT 11:13:15 ON 14 DEC 2006

FILE 'DRUG' ENTERED AT 11:13:15 ON 14 DEC 2006

COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'CAPLUS' ENTERED AT 11:13:15 ON 14 DEC 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE 'HELP USAGETERMS' FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPX' ENTERED AT 11:13:15 ON 14 DEC 2006

COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'EMBASE' ENTERED AT 11:13:15 ON 14 DEC 2006

Copyright (c) 2006 Elsevier B.V. All rights reserved.

PROCESSING COMPLETED FOR L217

PROCESSING COMPLETED FOR L215

PROCESSING COMPLETED FOR L213

PROCESSING COMPLETED FOR L216

PROCESSING COMPLETED FOR L214

L218 19 DUP REM L217 L215 L213 L216 L214 (0 DUPLICATES REMOVED)

ANSWERS '1-6' FROM FILE MEDLINE
ANSWERS '7-10' FROM FILE DRUG
ANSWERS '11-15' FROM FILE CAPLUS
ANSWERS '16-17' FROM FILE WPX
ANSWERS '18-19' FROM FILE EMBASE

=> d iall 1-10; d ibib ed abs hit 11-15; d ibib abeq tech hiters 16-17; d iall 18-19; fil hom

L218 ANSWER 1 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2006205320 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16612168
TITLE: Efficacy of controlled-release oxycodone for dyspnea in cancer patients--three case series.
AUTHOR: Shinjo Takuya; Okada Masakuni
CORPORATE SOURCE: Dept. of Palliative Care Unit, Shikaihoken Kobe Central Hospital.
SOURCE: Gan to kagaku ryoho. Cancer & chemotherapy, (2006 Apr) Vol. 33, No. 4, pp. 529-32.
Journal code: 7810034. ISSN: 0385-0684.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (CASE REPORTS)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 14 Apr 2006
Last Updated on STN: 10 May 2006
Entered Medline: 9 May 2006

ABSTRACT: Dyspnea is a common symptom in patients with advanced cancer. Systemic morphine administration has been reported as an effective pharmacological treatment to control dyspnea. However, there have been few reports on similar effects of alternative opioids except for morphine. To evaluate the effect of controlled-release oxycodone on the relief of dyspnea, we investigated three cases with opioid substitution from subcutaneous morphine to oral oxycodone. In all cases, both opioids provided equivalent effects for the palliation of cancer dyspnea with no significant adverse effects. Future studies in the appropriate clinical designs will be needed to confirm our findings.

CONTROLLED TERM: Check Tags: Female: Male
Administration, Oral
Aged
*Analgesics, Opioid: AD, administration & dosage
Delayed-Action Preparations
*Dyspnea: DT, drug therapy
Dyspnea: ET, etiology
English Abstract
Humans
Injections, Subcutaneous
Lung Neoplasms: CO, complications
*Lung Neoplasms: PP, physiopathology
Middle Aged
Morphine: AD, administration & dosage
*Oxycodone: AD, administration & dosage

CAS REGISTRY NO.: 57-27-2 (Morphine); 76-42-6 (Oxycodone)
CHEMICAL NAME: 0 (Analgesics, Opioid); 0 (Delayed-Action Preparations)

L218 ANSWER 2 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2005170167 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15801946

TITLE: Co-administration of oxycodone and morphine and analgesic synergy re-examined.
AUTHOR: Smith Marc T; de la Iglesia Felix A
SOURCE: British journal of clinical pharmacology, (2005 Apr) Vol. 59, No. 4, pp. 486-7; author reply 487-8.
Journal code: 7503323. ISSN: 0306-5251.
COMMENT: Comment on: Br J Clin Pharmacol. 2004 Sep;58(3):235-42.
PubMed ID: 15327582
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Commentary
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 2 Apr 2005
Last Updated on STN: 2 Aug 2005
Entered Medline: 1 Aug 2005
CONTROLLED TERM: *Analgesics, Opioid: AD, administration & dosage
*Cold
Drug Combinations
Drug Synergism
Humans
*Morphine: AD, administration & dosage
*Nociceptors: DE, drug effects
*Oxycodone: AD, administration & dosage
*Pain: PC, prevention & control
CAS REGISTRY NO.: 57-27-2 (Morphine); 76-42-6 (Oxycodone)
CHEMICAL NAME: 0 (Analgesics, Opioid); 0 (Drug Combinations)

L218 ANSWER 3 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2004422001 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15327582
TITLE: Can coadministration of oxycodone and morphine produce analgesic synergy in humans? An experimental cold pain study.
AUTHOR: Grach Michael; Massalha Wattan; Pud Dorit; Adler Rivka; Eisenberg Elon
CORPORATE SOURCE: Department of Anaesthesiology, Carmel Hospital, Haifa, Israel.
SOURCE: British journal of clinical pharmacology, (2004 Sep) Vol. 58, No. 3, pp. 235-42.
Journal code: 7503323. ISSN: 0306-5251.
COMMENT: Comment on: Br J Clin Pharmacol. 2005 Apr;59(4):486-7; author reply 487-8. PubMed ID: 15801946
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
JOURNAL: Article: (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 26 Aug 2004
Last Updated on STN: 20 Dec 2004
Entered Medline: 17 Dec 2004

ABSTRACT: The coadministration of subantinociceptive doses of oxycodone with morphine has recently been shown to result in a synergistic antinociceptive effect in rats. The present study was aimed to investigate the possibility that coadministration of morphine and oxycodone can produce a similar synergistic effect in humans exposed to an experimental model

10/661458

of cold pressor test (CPT). METHODS: The enriched enrollment design was used to exclude 'stoic' and 'placebo responders' in a single-blind fashion. 'Monotonic', placebo 'nonresponder' female volunteers (n = 30) were randomly assigned to receive 0.5 mg/kg(-1) oral morphine sulphate, 0.5 mg/kg(-1) oral oxycodone hydrochloride, and the combination of 0.25 mg/kg(-1) morphine sulphate with 0.25 mg/kg(-1) oxycodone hydrochloride, 1 week apart from each other, in a double-blind crossover design. Latency to pain onset (threshold), pain intensity (VAS), and pain tolerance (time until removal of the hand from the water) were measured six times over a 3-h period, subsequent to the administration of each medication, and were used to assess their antinociceptive effect. RESULTS: The combination produced a significantly higher effect on latency to pain onset than that of morphine alone [difference in mean postbaseline value 2.2; 95% confidence interval (CI) 0.48, 3.9; P = 0.01] but the effect was nonsignificantly smaller than that of oxycodone alone. Similarly, the effect of the combination on pain tolerance was significantly larger than that of morphine alone (combination difference 8.4; 95% CI 2.5, 14.3; P = 0.007), whereas oxycodone alone caused a nonsignificantly larger effect than that of the combination treatment. Comparisons of pain magnitude failed to show any significant differences between the three treatments. CONCLUSIONS: These results indicate that at the doses tested, morphine and oxycodone do not produce synergistic antinociceptive effects in healthy humans exposed to the CPT.

CONTROLLED TERM: Check Tags: Female

Adolescent
Adult
*Analgesics, Opioid; AD, administration & dosage
*Cold
Cross-Over Studies
Double-Blind Method
Drug Combinations
Drug Synergism
Humans
*Morphine; AD, administration & dosage
*Oxycodone; AD, administration & dosage
*Pain; PC, prevention & control
Research Support, Non-U.S. Gov't
57-27-2 (Morphine); 76-42-6 (Oxycodone)
0 (Analgesics, Opioid); 0 (Drug Combinations)

CAS REGISTRY NO.:

CHEMICAL NAME:

L218 ANSWER 4 OF 19

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

AUTHOR:

CORPORATE SOURCE:

CONTRACT NUMBER:

SOURCE:

PUB. COUNTRY:

DOCUMENT TYPE:

LANGUAGE:

MEDLINE on STN

2003606915 MEDLINE [Full-text](#)

PubMed ID: 14557380

Opioid interactions in rhesus monkeys: effects of delta + mu and delta + kappa agonists on schedule-controlled responding and thermal nociception.

Stevenson Glenn W; Folk John E; Linsmeyer David C; Rice Kenner C; Negus S Stevens
Alcohol and Drug Abuse Research Center, Harvard Medical School, McLean Hospital, 115 Mill St., Belmont, MA 02478-9106, USA.

P01-DA14528 (NIDA)

R01-DA11460 (NIDA)

T32-DA07252 (NIDA)

The Journal of pharmacology and experimental therapeutics, (2003 Dec) Vol. 307, No. 3, pp. 1054-64. Electronic Publication: 2003-10-13.

Journal code: 0376362. ISSN: 0022-3565.

United States

Journal; Article; (JOURNAL ARTICLE)

English

29

10/661458

FILE SEGMENT:

ENTRY MONTH:

ENTRY DATE:

Priority Journals

200401

Entered STN: 24 Dec 2003

Last Updated on STN: 30 Jan 2004

Entered Medline: 29 Jan 2004

ABSTRACT:

Agonists at delta, mu, and kappa opioid receptors produce interacting effects in rodents and nonhuman primates. To further evaluate the determinants of these interactions, this study examined the effects of mixtures of delta + mu and delta + kappa agonists in rhesus monkeys (n = 4-5) using two behavioral procedures, an assay of schedule-controlled responding for food reinforcement and an assay of thermal nociception. Results were analyzed using dose-addition analysis. In the assay of schedule-controlled responding, the delta agonist (+)-4-[[alphaR]-alpha-(2S,5R)-4-allyl-2,5-dimethyl-1-piperazinyl]-3-methoxybenzyl]-N,N-diethylbenzamide (SNC80); the mu agonists methadone, fentanyl, morphine, and nalbuphine; and the kappa agonists (alpha,7alpha,8beta)-(-)-N-methyl-N-(7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl) benzeneacetamide (U69,593) and brenazocine all dose dependently decreased rates of food-maintained responding when administered alone. Fixed ratio mixtures of SNC80 + mu agonists produced additive or subadditive effects, whereas SNC80 + kappa agonist mixtures produced only additive effects. In the assay of thermal nociception, SNC80 produced no measurable effects when administered alone, whereas mu and kappa agonists produced dose-dependent antinociception. SNC80 + mu agonist mixtures produced superadditive effects manifested as leftward shifts in mu agonist dose-effect curves. This synergism was antagonized by the delta-selective antagonist naltrindole, suggesting that SNC80-induced enhancement of mu agonist antinociception was delta receptor-mediated. SNC80 did not enhance the antinociceptive effects of the highly selective kappa agonist U69,593, and it produced only a marginal enhancement of antinociception produced by the less selective kappa agonist brenazocine. These results suggest that delta agonists may selectively enhance the antinociceptive effects of mu agonists in rhesus monkeys. These results also confirm that opioid agonist interactions may depend on the receptor selectivity and relative doses of the agonists and on the experimental endpoint.

CONTROLLED TERM:

Check Tags: Male

*Analgesics, Opioid; PD, pharmacology
Animals
Benzamides; PD, pharmacology
Benzeneacetamides; PD, pharmacology
Benzomorphanes; PD, pharmacology
*Conditioning, Operant; DR, drug effects
Dose-Response Relationship; Drug
Drug Interactions
Heat
Naloxone; AA, analogs & derivatives
Naltrexone; PD, pharmacology
Narcotic Antagonists; PD, pharmacology
*Pain; PX, psychology
Piperazines; PD, pharmacology
Pyrrolidines; PD, pharmacology
*Receptors, Opioid, delta; AG, agonists
*Receptors, Opioid, kappa; AG, agonists
*Receptors, Opioid, mu; AG, agonists
Reinforcement Schedule
Research Support, U.S. Gov't, P.H.S.
11555-53-4 (naltrindole); 156727-74-1 (4-(alpha-(4-allyl-2,5-dimethyl-1-piperazinyl)-3-methoxybenzyl)-N,N-diethylbenzamide); 16590-41-3 (Naltrexone); 75684-07-0 (brenazocine); 96744-75-1 (U 69593)

CAS REGISTRY NO.:

10/661458

10/661458

CHEMICAL NAME: 0 (Analgesics, Opioid); 0 (Benzamides); 0 (Benzeneacetamides); 0 (Benzomorphanes); 0 (Narcotic Antagonists); 0 (Piperazines); 0 (Pyrrolidines); 0 (Receptors, Opioid, delta); 0 (Receptors, Opioid, kappa); 0 (Receptors, Opioid, mu)

L218 ANSWER 5 OF 19

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

AUTHOR:

CORPORATE SOURCE:

SOURCE:

PUB. COUNTRY:

DOCUMENT TYPE:

LANGUAGE:

FILE SEGMENT:

ENTRY MONTH:

ENTRY DATE:

MEDLINE on STN

2000107229 MEDLINE [Full-text](#)

PubMed ID: 10640321

The antitussive activity of delta-opioid receptor stimulation in guinea pigs.

Kotzer C J; Hay D W; Dondio G; Giardina G; Petrillo P; Underwood D C

Department of Pulmonary Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, Pennsylvania, USA.

The Journal of pharmacology and experimental therapeutics, (2000 Feb) Vol. 292, No. 2, pp. 803-9.

Journal code: 0376362. ISSN: 0022-3565.

United States

Journal; Article; (JOURNAL ARTICLE)

English

Priority Journals

200002

Entered STN: 9 Mar 2000

Last Updated on STN: 9 Mar 2000

Entered Medline: 22 Feb 2000

ABSTRACT:

In this study, the activity of the delta-opioid receptor subtype-selective agonist, SB 271222, was investigated in a guinea pig model of citric acid-induced cough. Parenteral administration of selective agonists of the delta-opioid receptor (SB 271222), mu-opioid receptor (codeine and hydrocodone), and kappa-opioid receptor (BRL 52974) produced dose-related inhibition of citric acid-induced cough with ED(50) values of 7.3, 5.2, 5.1, and 5.3 mg/kg, respectively. The nonselective opioid receptor antagonist, naloxone (3 mg/kg, i.v.), attenuated the antitussive effects of codeine or SB 271222, indicating that the antitussive activity of both compounds is opioid receptor-mediated. The delta-receptor antagonist, SB 244525 (10 mg/kg, i.p.), inhibited the antitussive effect of SB 271222 (20 mg/kg, i.p.). In contrast, combined pretreatment with beta-naloxonium (mu-receptor antagonist; 20 mg/kg, s.c.) and naltrexamine (kappa-receptor antagonist; 20 mg/kg, s.c.), at doses that inhibited the antitussive activity of mu- and kappa-receptor agonists, respectively, was without effect on the antitussive response of SB 271222 (20 mg/kg, i.p.). The sigma-receptor antagonist rimcazole (3 mg/kg, i.p.) inhibited the antitussive effect of dextromethorphan (30 mg/kg, i.p.), a sigma-receptor agonist, but not that of SB 271222. These studies provide compelling evidence that the antitussive effects of SB 271222 in this guinea pig cough model are mediated by agonist activity at the delta-opioid receptor.

CONTROLLED TERM: Check Tags: Male

Animals
CHO Cells
Carbazoles; PD, pharmacology
Cell Line
Cloning, Organism
Codeine; PD, pharmacology
*Cough; PC, prevention & control
Cricetines
Dextromethorphan; PD, pharmacology
Disease Models, Animal
Dose-Response Relationship; Drug

Drug Interactions

Guinea Pig

Humans

Hydrocodone; PD, pharmacology

*Levallorphan; AA, analogs & derivatives

Levallorphan; TU, therapeutic use

Naloxone; PD, pharmacology

*Narcotic Antagonists; PD, pharmacology

Pyrrolidines; PD, pharmacology

*Pyrrolones; TU, therapeutic use

Pyrrolidines; PD, pharmacology

Receptors, Opioid, delta; AG, agonists

*Receptors, Opioid, delta; DE, drug effects

*Receptors, Opioid, delta; PH, physiology

Receptors, Opioid, kappa; AG, agonists

Receptors, Opioid, kappa; DE, drug effects

Receptors, Opioid, kappa; PH, physiology

Receptors, Opioid, mu; AG, agonists

Receptors, Opioid, mu; DE, drug effects

Receptors, Opioid, mu; PH, physiology

CAS REGISTRY NO.:

125-29-1 (Hydrocodone); 125-71-3 (Dextromethorphan); 145544-79-2 (BRL 52974); 152-02-3 (Levallorphan); 465-65-6 (Naloxone); 75859-04-0 (rimcazole); 76-57-3 (Codeine)
0 (Carbazoles); 0 (Narcotic Antagonists); 0 (Pyrrolidines); 0 (Pyrrolones); 0 (Pyrrolidines); 0 (Receptors, Opioid, delta); 0 (Receptors, Opioid, kappa); 0 (Receptors, Opioid, mu); 0 (SB 271222)

L218 ANSWER 6 OF 19

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

AUTHOR:

CORPORATE SOURCE:

SOURCE:

PUB. COUNTRY:

DOCUMENT TYPE:

LANGUAGE:

FILE SEGMENT:

ENTRY MONTH:

ENTRY DATE:

MEDLINE on STN

2000133083 MEDLINE [Full-text](#)

PubMed ID: 10666549

Co-administration of sub-antinociceptive doses of oxycodone and morphine produces marked antinociceptive synergy with reduced CNS side-effects in rats.

Ross P B; Wallis S C; Smith W T
School of Pharmacy, The University of Queensland, St Lucia, Brisbane, Australia.

Pain, (2000 Feb) Vol. 84, No. 2-3, pp. 421-8.

Journal code: 7508666. ISSN: 0304-3959.

Netherlands

Journal; Article; (JOURNAL ARTICLE)

English

Priority Journals

200003

Entered STN: 27 Mar 2000

Last Updated on STN: 27 Mar 2000

Entered Medline: 16 Mar 2000

ABSTRACT:

Oxycodone and morphine are structurally related, strong opioid analgesics, commonly used to treat moderate to severe pain in humans. Although it is well-established that morphine is a mu-opioid agonist, this is not the case for oxycodone. Instead, our recent studies have shown that oxycodone appears to be a kappa-opioid agonist (Ross and Smith, 1997). In the current study, we now show that co-administration of sub-antinociceptive doses of oxycodone (putative kappa-opioid agonist) with morphine (mu-opioid agonist) to rats by both the intracerebroventricular and by systemic routes (intraperitoneal and subcutaneous), results in markedly increased (synergistic) levels of antinociception. Behaviourally, rats co-administered sub-antinociceptive doses of oxycodone and morphine were similar to control rats dosed with saline,

31

32

whereas rats that received equi-potent doses of either opioid alone, were markedly sedated. These results suggest that co-administration of sub-analgesic doses of oxycodone and morphine to patients may provide excellent pain relief with a reduction in opioid-related CNS side-effects. Controlled clinical trials in appropriate patient populations are required to evaluate this possibility. (1)

CONTROLLED TERM: Check Tags: Male
 Analgesics, Opioid: AD, administration & dosage
 Analgesics, Opioid: PD, pharmacology
 Animals
 Behavior, Animal: DR, drug effects
 Central Nervous System: DR, drug effects
 Dose-Response Relationship, Drug
 Drug Combinations
 Drug Synergism
 Injections, Intraperitoneal
 Injections, Intraventricular
 Injections, Subcutaneous
 Morphine: AD, administration & dosage
 Morphine: PD, pharmacology
 Nociceptors: DR, drug effects
 Oxycodone: AD, administration & dosage
 Oxycodone: PD, pharmacology
 Rate
 Rate, Sprague-Dawley
 Research Support, Non-U.S. Gov't
 CAS REGISTRY NO.: 57-27-2 (Morphine); 76-42-6 (Oxycodone)
 CHEMICAL NAME: 0 (Analgesics, Opioid); 0 (Drug Combinations)

L218 ANSWER 7 OF 19 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN
 ACCESSION NUMBER: 1995-21708 DRUGU T Full-text
 TITLE: A pain syndrome associated with large adrenal masses in patients with lung cancer.
 AUTHOR: Berger M S; Cooley M E; Abraham J L
 CORPORATE SOURCE: Univ. Pennsylvania
 LOCATION: Philadelphia, Pa., USA
 SOURCE: J. Pain Symptom Manage. (10, No. 2, 161-66, 1995) 2 Fig. 13
 Ref.
 CODEN: JPSMKU ISSN: 0885-3924
 AVAIL. OF DOC.: Hematology-Oncology Division, Philadelphia VA Medical Center,
 University and Woodlands Avenues, Philadelphia, PA. U.S.A.
 LANGUAGE: English
 DOCUMENT TYPE: Journal

ABSTRACT:

Case histories are reported of 2 patients with lung cancer who had a pain syndrome caused by large adrenal metastases. Patient 1 had a poor response to radiation, controlled-release p.o. morphine and acetaminophen-oxycodone. He responded to chemotherapy with cyclophosphamide (Cytosan), Adriamycin and vincristine (CAV). He was given hydrocortisone for orthostatic hypotension. Hip pain developed and he died. Patient 2 was treated with controlled-release p.o. morphine but pain progressed and he died. 23 Previously recorded cases were reviewed.

SECTION HEADING: T Therapeutics

CLASSIF. CODE: 43 Analgesics, NSAIDs
44 Narcotics

CONTROLLED TERM:

ADRENAL *TR; METASTASIS *TR; ADRENOPATHY *TR; NEOPLASM *TR;
 PAIN *TR; LUNG *OC; SMALL-CELL *OC; LARGE-CELL *OC; NEOPLASM
 *OC; HYDROCORTISONE *RC; CASE-HISTORY *FT; IN-VIVO *FT;
 RADIOTHERAPY *FT; CONCOMITANT-DISEASE *FT; EXITUS *FT; CASES
 *FT
 [01] MORPHINE *TR; MORPHINE *RN; ANALGESIC
 *FT; DEPOT *FT; P.O. *FT; PHARM.PREP. *FT; ANALGESICS *FT;
 NARCOTICS *FT; SEDATIVES *FT; 57-27-2 *FT; TR *FT
 CAS REGISTRY NO.: 57-27-2
 [02] OXYCODONE *TR; OXYCODONE *RN; COMB.PREP.
 *FT; P.O. *FT; ANALGESIC *FT; ANALGESICS *FT; NARCOTICS *FT;
 SEDATIVES *FT; 76-42-6 *FT; TR *FT
 CAS REGISTRY NO.: 76-42-6
 [03] PARACETAMOL *TR; PARACETAM *RN; COMB.PREP. *FT; ANALGESIC
 *FT; P.O. *FT; ANALGESICS *FT; ANTIPIREPTICS *FT; 103-90-2
 *FT; TR *FT
 CAS REGISTRY NO.: 103-90-2
 [04] CYCLOPHOSPHAMIDE *TR; CYTOXAN *TR; CYCLOPHOS *RN; CYTOSTATIC
 *FT; CYTOSTATIC-COMB. *FT; COMB. *FT; CYTOSTATICS
 *FT; IMMUNOSUPPRESSIVES *FT; 50-18-0 *FT; TR *FT
 CAS REGISTRY NO.: 50-18-0
 [05] DOXORUBICIN *TR; ADRIAMYCIN *TR; DOXORUBIC *RN; CYTOSTATIC
 *FT; CYTOSTATIC-COMB. *FT; COMB. *FT; ANTIBIOTICS
 *FT; CYTOSTATICS *FT; 23214-92-8 *FT; TR *FT
 CAS REGISTRY NO.: 23214-92-8
 [06] VINCISTINE *TR; VINCISTI *RN; CYTOSTATIC *FT;
 CYTOSTATIC-COMB. *FT; COMB. *FT; CYTOSTATICS *FT;
 57-22-7 *FT; TR *FT
 CAS REGISTRY NO.: 57-22-7
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature

L218 ANSWER 8 OF 19 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN
 ACCESSION NUMBER: 1993-55507 DRUGU T S Full-text
 TITLE: A Risk-Benefit Appraisal of Injectable NSAIDs in the Management of Postoperative Pain.
 AUTHOR: Nuutinen L S; Laitinen J O; Salomaki T E
 LOCATION: Kuopio, Oulu, Finland
 SOURCE: Drug Safety (19, No. 5, 380-93, 1993) 3 Tab. 124 Ref.
 ISSN: 0114-5916
 AVAIL. OF DOC.: Department of Anaesthesiology, University Hospital, P.O.8
 1777, SF-70211 Kuopio, Finland.
 LANGUAGE: English
 DOCUMENT TYPE: Journal

ABSTRACT:

Injectable NSAIDs in the management of postoperative pain are reviewed, with reference to their mode of action, the use of indometacin (IN), diclofenac (DI), ketorolac (KE) and other NSAIDs for acute pain, the adverse effects of NSAIDs on the GI system, coagulation and renal and other adverse effects. Somnolence, dry mouth and GI effects are the commonest adverse events with KE. Interactions occur between NSAIDs and anticoagulants, diuretics, beta-blockers and lithium. Parenteral NSAIDs, particularly IN, DI and KE, have a clear role in the management of postoperative pain. Their efficacy is well proved in orthopedic surgery. Their use is contraindicated in patients with a history of

asthma, allergy, renal pathology or peptic ulceration.

SECTION HEADING: T Therapeutics
S Adverse EffectsCLASSIF. CODE: 35 Adverse Reactions
43 Analgesics, NSAIDs
44 Narcotics
66 Drug Interactions
69 Reviews

CONTROLLED TERM:

PAIN *TR; POSTOPERATIVE *TR; IN-VIVO *FT; CASES *FT;
 INJECTION *FT; ANTIINFLAMMATORY *FT; REVIEW *FT; RISK-FACTOR
 *FT
 [01] ANTIINFLAMMATORIES *FT; MAIN-TOPIC *FT; TR *FT; AE *FT; DI
 *FT
 [02] INDOMETACIN *TR; INDOMETACIN *AE; DICLOFENAC *AE; DICLOFENAC
 *TR; KETOROLAC *TR; KETOROLAC *AE; INDOMETACIN *DI;
 DICLOFENAC *DI; KETOROLAC *DI; OXYCODONE *TR;
 PETHIDINE *TR; PENTANYL *TR; MORPHINE
 *TR; PAPAVERETUM *TR; MORPHINE *AE;
 ASPIRIN-LYSINE-SALT *TR; KETOPROFEN *TR; INDOPROFEN *TR;
 TENOXICAM *TR; PIROXICAM *AE; OXYCODONE *AE;
 PENTANYL *AE; ASPIRIN *AE; ALFENTANIL *AE;
 MODE-OF-ACT. *FT; ORTHOPEDICS *FT; SURGERY *FT;
 CONTRAINDICATION *FT; DRUG-COMPARISON *FT; I.V. *FT;
 INJECTION *FT; TR *FT; AE *FT; DI *FT
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature

L218 ANSWER 9 OF 19 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STN
 ACCESSION NUMBER: 1991-28479 DRUGU S Full-text
 TITLE: A Prospective Study of Hospital Admissions Due to Drug Reactions.
 AUTHOR: Leamur I; Dolphin R O; Saxter H; Morrison S; Hooke D H;
 McGrath S P
 LOCATION: Melbourne, Australia
 SOURCE: Aust. J. Hosp. Pharm. (21, No. 2, 90-95, 1991) 2 Fig. 4 Tab. 14
 Ref.
 CODEN: AUNPAI ISSN: 0310-6810
 AVAIL. OF DOC.: Manager of Pharmaceutical Services, Monash Medical Center,
 Prince Henry's Hospital, St. Kilda Road, Melbourne, Vic.
 3004, Australia.
 LANGUAGE: English
 DOCUMENT TYPE: Journal

ABSTRACT:

67 Drugs were implicated in adverse drug reactions (ADRs) in 136/5423 hospital admissions (2.4%) in a 6-mth prospective study. Drugs included piroxicam, diclofenac, indomethacin, diflunisal, ketoprofen, naproxen, cimetidine, doxycycline, warfarin, aspirin, dipyridamole, hydralazine, cyclopenthiadiazole, atenolol, metoprolol, digoxin, amiodarone, verapamil, nifedipine, chlorothalidate, methylglucamine, theophylline, allopurinol, ranitidine, methotrexate, glibenclamide, metformin, prochlorperazine, oxycodone, bromocriptine, thioridazine, naproxen, bleomycin, promethazine, morphine, allopurinol, co-trimoxazole, (trimethoprim + sulfamethoxazole), cyclophosphamide. Most ADRs were GI bleeding and cardiovascular complications;

5 were fatal.

SECTION HEADING: S Adverse Effects

CLASSIF. CODE: 18 Hematological
35 Adverse Reactions
43 Analgesics, NSAIDs
58 Vasoactive
66 Drug Interactions

CONTROLLED TERM:

IN-VIVO *FT; CASES *FT; COMB. *FT
 [01] CYCLOPHOSPHAMIDE *AE; CYCLOPHOSPHAMIDE *DI; PANCYTOPENIA *AE;
 MARROW-DISEASE *AE; HEMOPTYSIS *AE; HEMORRHAGE *AE; CYSTITIS
 *AE; BLADDER-DISEASE *AE; WARFARIN *DI; ASPIRIN *DI;
 CYTOSTATICS *FT; IMMUNOSUPPRESSIVES *FT; CYCLOPHOS *RN; AE
 *FT; DI *FT
 CAS REGISTRY NO.: 50-18-0
 [02] WARFARIN *DI; WARFARIN *AE; PANCYTOPENIA *AE; MARROW-DISEASE
 *AE; HEMOPTYSIS *AE; HEMORRHAGE *AE; CYSTITIS *AE;
 HEMATEMESIS *AE; MELENA *AE; GASTROENTEROPATHY *AE;
 HEMORRHAGE *AE; EMBUSIS *AE; GASTROENTEROPATHY *AE;
 DEHYDRATION *AE; ANEMIA *AE; BLADDER-DISEASE *AE;
 TRIMETHOPRIM *DI; DOXYCYCLINE *DI; SULFAMETHOXAZOLE *DI;
 ASPIRIN *DI; PREDNISOLONE *DI; CIMETIDINE *DI;
 CYCLOPHOSPHAMIDE *DI; RODENTICIDES *FT; ANTICOAGULANTS *FT;
 WARFARIN *RN; DI *FT; AE *FT
 CAS REGISTRY NO.: 5543-58-8
 [03] ASPIRIN *DI; ASPIRIN *AE; PANCYTOPENIA *AE; MARROW-DISEASE
 *AE; HEMOPTYSIS *AE; HEMORRHAGE *AE; CYSTITIS *AE;
 HEMATEMESIS *AE; MELENA *AE; GASTROENTEROPATHY *AE;
 HEMORRHAGE *AE; ANEMIA *AE; BLADDER-DISEASE *AE; DICLOFENAC
 *DI; DIFLUNISAL *DI; DIPPYRIDAMOLE *DI; INDOMETACIN *DI;
 KETOPROFEN *DI; NAPROXEN *DI; PIROXICAM *DI; WARFARIN *DI;
 PREDNISOLONE *DI; CYCLOPHOSPHAMIDE *DI; ANALGESICS *FT;
 ANTIPIREPTICS *FT; ANTIRHEUMATICS *FT; ANTIAGGREGANTS *FT;
 PROSTAGLANDIN-ANTAGONISTS *FT; ASPIRIN *RN; DI *FT; AE *FT
 CAS REGISTRY NO.: 50-78-2
 [04] TRIMETHOPRIM *DI; TRIMETHOPRIM *AE; HEMATEMESIS *AE; ANEMIA
 *AE; CEREBROVASCULAR-DISEASE *AE; MELENA *AE;
 GASTROENTEROPATHY *AE; HEMORRHAGE *AE; EMBUSIS *AE;
 GASTROENTEROPATHY *AE; DEHYDRATION *AE; MUCOSITIS *AE;
 WARFARIN *DI; CIMETIDINE *DI; DOXYCYCLINE *DI; ASPIRIN *DI;
 PREDNISOLONE *DI; CYCLOPHOSPHAMIDE *DI; METHOTREXATE *DI;
 COMB.PREP. *FT; ANTISEPTICS *FT; POLATE-ANTAGONISTS *FT;
 TRIMETHOP *RN; DI *FT; AE *FT
 CAS REGISTRY NO.: 738-70-5
 [05] SULFAMETHOXAZOLE *AE; HEMATEMESIS *AE; ANEMIA *AE;
 CEREBROVASCULAR-DISEASE *AE; MELENA *AE; GASTROENTEROPATHY
 *AE; HEMORRHAGE *AE; EMBUSIS *AE; GASTROENTEROPATHY *AE;
 DEHYDRATION *AE; MUCOSITIS *AE; WARFARIN *DI; CIMETIDINE *DI;
 DOXYCYCLINE *DI; ASPIRIN *DI; PREDNISOLONE *DI;
 CYCLOPHOSPHAMIDE *DI; METHOTREXATE *DI; COMB.PREP. *FT;
 ANTISEPTICS *FT; SULFETOXA *RN; AE *FT
 CAS REGISTRY NO.: 723-46-6
 [06] DICLOFENAC *AE; DICLOFENAC *DI; HEMATEMESIS *AE; MELENA *AE;
 GASTROENTEROPATHY *AE; HEMORRHAGE *AE; ANEMIA *AE; HEMOPTYSIS
 *AE; HEMORRHAGE *AE; ASPIRIN *DI; ANTIINFLAMMATORIES *FT;
 ANALGESICS *FT; PROSTAGLANDIN-ANTAGONISTS *FT; DICLOFENAC *RN;
 AE *FT; DI *FT

CAS REGISTRY NO.: 15307-86-5
[07] BLEOMYCIN *AE; PULMONARY-FIBROSIS *AE;
PNEUMOPATHY *AE; NEUTROPENIA *AE; MARROW-DISEASE *AE;
THROMBOCYTOPENIA *AE; ANTIBIOTICS *FT; CYTOSTATICS *FT;
BLEOMYCIN *RN; AE *FT

CAS REGISTRY NO.: 11056-06-7
[08] NAPROXEN *AE; HEMATEMESIS *AE; MELENA *AE; GASTROENTEROPATHY
*AE; HEMORRHOAGE *AE; PROSTAGLANDIN-ANTAGONISTS *FT;
ANTIINFLAMMATORIES *FT; ANALGESICS *FT; ANTIPIRETTICS *FT;
NAPROXEN *RN; AE *FT

CAS REGISTRY NO.: 22204-53-1
[09] DIGOXIN *DI; DIGOXIN *AE; BRADYCARDIA *AE; ANOREXIA *AE;
HEART-BLOCK *AE; ARRHYTHMIA *AE; CARDIOPATHY *AE; AMIODARONE
*DI; VERAPAMIL *DI; ATENOLOL *DI; NIFEDIPINE *DI;
CARDIOGLYCOSIDES *FT; CARDIANTS *FT; DIGOXIN *RN; DI *FT; AE
*FT

CAS REGISTRY NO.: 20830-75-5
[10] CIMETIDINE *AE; CIMETIDINE *DI; HEMATEMESIS *AE; ANEMIA *AE;
CEREBROVASCULAR-DISEASE *AE; WARFARIN *DI; TRIMETHOPRIM *DI;
SULFAMETHOXAZOLE *DI; ANTIHISTAMINES-H2 *FT; ANTIULCERS *FT;
GASTRIC-SECRETION-INHIBITORS *FT; CIMETIDIN *RN; AE *FT; DI
*FT

CAS REGISTRY NO.: 151481-61-9
[11] AMIODARONE *DI; AMIODARONE *AE; BRADYCARDIA *AE; ARRHYTHMIA
*AE; CARDIOPATHY *AE; ANOREXIA *AE; DIGOXIN *DI; VERAPAMIL
*DI; CALCIUM-ANTAGONISTS *FT; CARDIANTS *FT; ANTIARRHYTHMICS
*FT; AMIODARON *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 1951-25-3
[12] VERAPAMIL *DI; VERAPAMIL *AE; ARRHYTHMIA *AE; CARDIOPATHY
*AE; ANOREXIA *AE; DIGOXIN *DI; AMIODARONE *DI; CARDIANTS
*FT; CALCIUM-ANTAGONISTS *FT; VERAPAMIL *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 52-53-9
[13] ATENOLOL *DI; ATENOLOL *AE; HEART-BLOCK *AE; ARRHYTHMIA *AE;
CARDIOPATHY *AE; DIGOXIN *DI; NIFEDIPINE *DI;
SYMPATHOLYTICS-BETA *FT; HYPOTENSIVES *FT; ATENOLOL *RN; DI
*FT; AE *FT

CAS REGISTRY NO.: 29132-68-7
[14] NIFEDIPINE *DI; NIFEDIPINE *AE; BRADYCARDIA *AE; ARRHYTHMIA
*AE; CARDIOPATHY *AE; DIGOXIN *DI; ATENOLOL *DI; CARDIANTS
*FT; CALCIUM-ANTAGONISTS *FT; NIFEDIPIN *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 21829-25-4
[15] METHYLDOPA *DI; METHYLDOPA *AE; ORTHOSTATIC *AE; HYPOTENSION
*AE; VASCULAR-DISEASE *AE; PERIPHERAL-NERVE-DISEASE *AE;
CHLOROTHIAZIDE *DI; VERAPAMIL *DI; CHLOROPROMAZINE *DI;
HYDRALAZINE *DI; HYPOTENSIVES *FT; SYMPATHOMIMETICS-ALPHA
*FT; METHYLDOP *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 555-10-6
[16] CHLOROTHIAZIDE *DI; CHLOROTHIAZIDE *AE; ORTHOSTATIC *AE;
HYPOTENSION *AE; VASCULAR-DISEASE *AE; PERIPHERAL-NERVE-
DISEASE *AE; METHYLDOPA *DI; VERAPAMIL *DI; CHLOROPROMAZINE
*DI; CARBONIC-ANHYDRASE-INHIBITORS *FT; DIURETICS *FT;
HYPOTENSIVES *FT; CHLOROTH *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 58-94-6
[17] CHLOROPROMAZINE *DI; CHLOROPROMAZINE *AE; ORTHOSTATIC *AE;
HYPOTENSION *AE; VASCULAR-DISEASE *AE; PERIPHERAL-NERVE-
DISEASE *AE; METHYLDOPA *DI; CHLOROTHIAZIDE *DI; VERAPAMIL
*DI; HYDRALAZINE *DI; PSYCHOSEDATIVES *FT; NEUROLEPTICS *FT;
SEDATIVES *FT; DOPAMINE-ANTAGONISTS *FT; CALMODULIN-
ANTAGONISTS *FT; CHLORPROM *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 50-53-3

37

[18] HYDRALAZINE *DI; HYDRALAZINE *AE; ORTHOSTATIC *AE;
HYPOTENSION *AE; VASCULAR-DISEASE *AE; PERIPHERAL-NERVE-
DISEASE *AE; METHYLDOPA *DI; VERAPAMIL *DI; CHLOROPROMAZINE
*DI; METOPROLOL *DI; CYCLOPENTHAZIDE *DI; HYPOTENSIVES *FT;
HYDRALAZI *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 86-54-4
[19] CYCLOPENTHAZIDE *DI; CYCLOPENTHAZIDE *AE; ORTHOSTATIC *AE;
HYPOTENSION *AE; VASCULAR-DISEASE *AE; ANEMIA *AE; PIROXICAM
*DI; ANALGESICS *FT; ANTIINFLAMMATORIES *FT; ANTIPIRETTICS
*FT; PROSTAGLANDIN-ANTAGONISTS *FT; DIPLUNISA *RN; DI *FT; AE
*FT

CAS REGISTRY NO.: 742-20-1
[20] DIPLUNISAL *DI; DIPLUNISAL *AE; HEMATEMESIS *AE; MELENA *AE;
GASTROENTEROPATHY *AE; HEMORRHOAGE *AE; ANEMIA *AE; PIROXICAM
*DI; ANALGESICS *FT; ANTIINFLAMMATORIES *FT; ANTIPIRETTICS
*FT; PROSTAGLANDIN-ANTAGONISTS *FT; DIPLUNISA *RN; DI *FT; AE
*FT

CAS REGISTRY NO.: 22494-42-4
[21] PIROXICAM *DI; PIROXICAM *AE; HEMATEMESIS *AE; MELENA *AE;
GASTROENTEROPATHY *AE; HEMORRHOAGE *AE; ANEMIA *AE; PIROXICAM
*DI; ANTIINFLAMMATORIES *FT; PROSTAGLANDIN-ANTAGONISTS *FT;
PIROXICAM *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 36323-30-4
[22] METOPROLOL *DI; METOPROLOL *AE; ORTHOSTATIC *AE; HYPOTENSION
*AE; VASCULAR-DISEASE *AE; PERIPHERAL-NERVE-DISEASE *AE;
CYCLOPENTHAZIDE *DI; HYDRALAZINE *DI; SYMPATHOLYTICS-BETA
*FT; METOPROLO *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 37350-58-6
[23] DIPYRIDAMOLE *DI; DIPYRIDAMOLE *AE; MELENA *AE;
GASTROENTEROPATHY *AE; HEMORRHOAGE *AE; ANEMIA *AE; ASPIRIN
*DI; CARDIANTS *FT; CALCIUM-ANTAGONISTS *FT; ANTIAGGREGANTS
*FT; PHOSPHODIESTERASE-INHIBITORS *FT; DIPYRIDAM *RN; DI *FT;
AE *FT

CAS REGISTRY NO.: 58-32-2
[24] INDOMETACIN *DI; INDOMETACIN *AE; MELENA *AE;
GASTROENTEROPATHY *AE; HEMORRHOAGE *AE; ASPIRIN *DI;
ANTIINFLAMMATORIES *FT; ANTIPIRETTICS *FT; ANTIRHEUMATICS
*FT; PROSTAGLANDIN-ANTAGONISTS *FT; INDOMETAC *RN; DI *FT; AE
*FT

CAS REGISTRY NO.: 53-66-1
[25] KETOPROFEN *DI; KETOPROFEN *AE; MELENA *AE; GASTROENTEROPATHY
*AE; HEMORRHOAGE *AE; ANEMIA *AE; ASPIRIN *DI;
ANTIINFLAMMATORIES *FT; ANALGESICS *FT; PROSTAGLANDIN-
ANTAGONISTS *FT; KETOPROFE *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 22071-15-4
[26] DOXYCYCLINE *DI; DOXYCYCLINE *AE; HEMATEMESIS *AE; MELENA
*AE; GASTROENTEROPATHY *AE; HEMORRHOAGE *AE; EMESIS *AE;
GASTROENTEROPATHY *AE; DEHYDRATION *AE; WARFARIN *DI;
TRIMETHOPRIM *DI; SULFAMETHOXAZOLE *DI; ANTIMOTICS *FT;
DOXYCYCLI *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 564-25-0
[27] PREDNISOLONE *DI; PREDNISOLONE *AE; HEMATEMESIS *AE; MELENA
*AE; GASTROENTEROPATHY *AE; HEMORRHOAGE *AE; ANEMIA *AE;
WARFARIN *DI; ASPIRIN *DI; CORTICOSTEROIDS *FT; PDNISOLON
*RN; DI *FT; AE *FT

CAS REGISTRY NO.: 50-24-0
[28] THEOPHYLLINE *DI; THEOPHYLLINE *AE; NAUSEA *AE; EMESIS *AE;
GASTROENTEROPATHY *AE; DEHYDRATION *AE; ALLOPURINOL *DI;
RANITIDINE *DI; BRONCHODILATORS *FT; VASODILATORS *FT;
CARDIANTS *FT; DIURETICS *FT; ANTIASTHMATICS *FT;
PHOSPHODIESTERASE-INHIBITORS *FT; THEOPHYLL *RN; DI *FT; AE
*FT

38

[29] *FT
ALLOPURINOL *DI; ALLOPURINOL *AE; NAUSEA *AE; EMESIS *AE;
GASTROENTEROPATHY *AE; THEOPHYLLINE *DI; ANTIGOUTS *FT;
ANTIINFLAMMATORIES *FT; ALLOPURIN *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 315-30-0
[30] RANITIDINE *DI; RANITIDINE *AE; ANOREXIA *AE; NAUSEA *AE;
EMESIS *AE; GASTROENTEROPATHY *AE; THEOPHYLLINE *DI;
ANTIINFLAMMATORIES *FT; ANTIGOUTS *FT; GASTRIC-SECRETION-
INHIBITORS *FT; RANITIDIN *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 66387-16-5
[31] METHOTREXATE *DI; METHOTREXATE *AE; MUCOSITIS *AE;
TRIMETHOPRIM *DI; SULFAMETHOXAZOLE *DI; CYTOSTATICS *FT;
METHOTREX *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 59-05-2
[32] GLIBENCLAMIDE *DI; GLIBENCLAMIDE *AE; HYPOGLYCEMIA *AE;
CARBOHYDRATE-METAB.DISORDER *AE; CONFUSION *AE;
MENTAL-DISORDER *AE; METFORMIN *DI; ANTIDIABETICS *FT;
GLIBENCLA *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 10238-21-8
[33] METFORMIN *DI; METFORMIN *AE; HYPOGLYCEMIA *AE;
CARBOHYDRATE-METAB.DISORDER *AE; CONFUSION *AE;
MENTAL-DISORDER *AE; GLIBENCLAMIDE *DI; ANTIDIABETICS *FT;
METFORMIN *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 657-24-9
[34] PROMETHAZINE *DI; PROMETHAZINE *AE; DYSTONIA *AE; MYOPATHY
*AE; EXTRAPYRAMIDAL-DISORDER *AE; ENCEPHALOPATHY *AE;
PROCHLORPERAZINE *DI; ANTIHISTAMINES-H1 *FT; SEDATIVES *FT;
PROMETHAZ *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 60-87-7
[35] PROCHLORPERAZINE *DI; PROCHLORPERAZINE *AE; DYSTONIA *AE;
MYOPATHY *AE; EXTRAPYRAMIDAL-DISORDER *AE; ENCEPHALOPATHY
*AE; PROMETHAZINE *DI; PSYCHOSEDATIVES *FT; NEUROLEPTICS *FT;
ANTISMETICS *FT; DOPAMINE-ANTAGONISTS *FT; PROCHLORP *RN; DI
*FT; AE *FT

CAS REGISTRY NO.: 58-38-5
[36] MORPHINE *DI; MORPHINE *AE; CONFUSION
*AE; MENTAL-DISORDER *AE; DROWSINESS *AE; OXYCODONE
*DI; ANALGESICS *FT; NARCOTICS *FT; SEDATIVES *FT;
MORPHINE *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 57-27-2
[37] OXYCODONE *DI; OXYCODONE *AE; CONFUSION
*AE; MENTAL-DISORDER *AE; DROWSINESS *AE; MORPHINE
*DI; ANALGESICS *FT; NARCOTICS *FT; SEDATIVES *FT;
OXYCODONE *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 74-42-6
[38] BROMOCRIPTINE *DI; BROMOCRIPTINE *AE; CONFUSION *AE;
MENTAL-DISORDER *AE; DROWSINESS *AE; THIORIDAZINE *DI;
ANTIPARKINSONIANS *FT; PROLACTIN-ANTAGONISTS *FT;
DOPAMINERGICS *FT; BROMOCRIPT *RN; DI *FT; AE *FT

CAS REGISTRY NO.: 25614-03-3
[39] THIORIDAZINE *DI; THIORIDAZINE *AE; CONFUSION *AE;
MENTAL-DISORDER *AE; DROWSINESS *AE; BROMOCRIPTINE *DI;
PSYCHOSEDATIVES *FT; NEUROLEPTICS *FT; DOPAMINE-ANTAGONISTS
*FT; CALMODULIN-ANTAGONISTS *FT; THIORIDAZ *RN; DI *FT; AE
*FT

CAS REGISTRY NO.: 50-52-2
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L218 ANSWER 10 OF 19 DRUGU COPYRIGHT 2006 THE THOMSON CORP ON STM

39

ACCESSION NUMBER: 1988-10343 DRUGU T P S Full-text
TITLE: Pain and Analgesics.
AUTHOR: Kurz H von
LOCATION: Munich, Germany, West
SOURCE: Dtsch.Apoth.Ztg. (127, No. 52-53, 2747-57, 1987) 6 Fig. 10
Tab. 20 Ref.
CODEN: DAZE2 ISSN: 0011-9857
Walthers-Straub-Institut fuer Pharmakologie und Toxikologie
Nussbaumstrasse 26, 8000 Muenchen 2, West Germany.
LANGUAGE: German
DOCUMENT TYPE: Journal
ABSTRACT:

The use of analgesics in the relief of pain is reviewed with reference to the
opioids and NSAID, their indications, mechanism of activity, pharmacokinetics,
dosage, side effects and interactions with other drugs. Agents that can elicit
attacks of asthma, that interact with salicylates and that can be
present in analgesic combinations without having analgesic properties are
listed. The most serious danger of using opioids are respiratory paralysis
after high doses of addiction following chronic use. NSAID have few side
effects when taken sensibly, though they can occasionally induce asthma
, Lyell's syndrome and possibly Reye's syndrome.

SECTION HEADING: T Therapeutics
P Pharmacology
S Adverse Effects
CLASSIF. CODE: 8 Pharmacokinetics
35 Adverse Reactions
43 Analgesics, NSAIDs
44 Narcotics
66 Drug Interactions
69 Reviews

CONTROLLED TERM:
[01] PAIN *TR; ANALGESIC *FT; REVIEW *FT; CASES *FT; IN-VIVO *FT
ANALGESICS *FT; MAIN-TOPIC *FT; TR *FT; PH *FT; DM *FT; AE
*FT; DI *FT
[02] PHENACETIN *AE; PHENACETIN *PH; PHENACETIN *DI; PARACETAMOL
*TR; PARACETAMOL *PH; PARACETAMOL *DM; PARACETAMOL *DI;
PARACETAMOL *AE; BUCETIN *TR; BUCETIN *DI; BUCETIN *DM;
BUCETIN *AE; BUCETIN *PH; PROPYPHENAZONE *TR; PROPYPHENAZONE
*AE; ISOPYRIN *PH; ISOPROPYLAMINOPHENAZONE *PH;
PROPYPHENAZONE *DI; PROPYPHENAZONE *DM; PROPYPHENAZONE *PH;
PHENAZONE *TR; PHENAZONE *AE; PHENAZONE *DM; PHENAZONE *DI;
PHENAZONE *PH; ISOPYRIN *TR; ISOPROPYLAMINOPHENAZONE *TR;
ISOPYRIN *AE; ISOPROPYLAMINOPHENAZONE *AE; ISOPYRIN *DM;
ISOPROPYLAMINOPHENAZONE *DM; ISOPYRIN *DI;
ISOPROPYLAMINOPHENAZONE *DI; METAMIZOLE *TR; METAMIZOLE *PH;
METAMIZOLE *DI; METAMIZOLE *DM; METAMIZOLE *AE; IBUPROFEN
*TR; IBUPROFEN *PH; IBUPROFEN *DM; IBUPROFEN *AE; IBUPROFEN
*DI; AZAPROPAZONE *AE; DICLOFENAC *AE; TR *FT; AE *FT; PH
*FT; DI *FT; DM *FT
[03] SALICYLATE *DM; SALICYLATE *AE; SALICYLATE *DI; ASPIRIN *TR;
ASPIRIN *AE; ASPIRIN *PH; ASPIRIN *DM; ASPIRIN *DI;
SALICYLAMIDE *TR; SALICYLAMIDE *PH; SALICYLAMIDE *AE;
SALICYLAMIDE *DM; SALICYLAMIDE *DI; ETHENZAMIDE *TR;
ETHENZAMIDE *AE; ETHENZAMIDE *PH; ETHENZAMIDE *DM;
ETHENZAMIDE *DI;

40

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

[04] ETHENZAMIDE *DM; SALACETAMIDE *TR; SALACETAMIDE *PH;
SALACETAMIDE *DI; SALACETAMIDE *DM; SALACETAMIDE *AR;
BENORILATE *TR; BENORILATE *DM; BENORILATE *AR; BENORILATE
*DI; BENORILATE *PH; DIFLUNISAL *TR; DIFLUNISAL *PH;
DIFLUNISAL *AR; DIFLUNISAL *DI; DIFLUNISAL *DM; PHENACETIN
*TR; PHENACETIN *DM; TR *FT; AR *FT; PH *FT; DM *FT; DI *FT
LEVOMETHADONE *PH; NEFOPAM *TR; NEFOPAM *AR; NEFOPAM *DI;
NEFOPAM *DI; OXYCODONE *DM;
OXYCODONE *PH; OXYCODONE *AR; PENTAZOCINE
*PH; PENTAZOCINE *TR; PENTAZOCINE *AR; PENTAZOCINE *DI;
PENTAZOCINE *DM; PETHIDINE *TR; PETHIDINE *AR; PETHIDINE *PH;
PETHIDINE *DI; PETHIDINE *DM; PIRITRAMIDE *TR; PIRITRAMIDE
*AR; PIRITRAMIDE *DM; PIRITRAMIDE *DI; PIRITRAMIDE *PH;
TILIDINE *TR; TILIDINE *AR; TILIDINE *PH; TILIDINE *DI;
TILIDINE *DM; TRAMADOL *TR; TRAMADOL *AR; TRAMADOL *PH;
TRAMADOL *DI; TRAMADOL *DM; SALICYLATE *TR; DIACETYLMORPHINE
*TR; DIACETYLMORPHINE *DM; DIACETYLMORPHINE *PH;
DIACETYLMORPHINE *DM; DIACETYLMORPHINE *DI; SALICYLATE *PH;
TR *FT; PH *FT; DI *FT; AR *FT; DM *FT
[05] SUPRENORPHINE *TR; CODEINE *TR; DEXTROPROPOXYPHENE *TR;
SUPRENORPHINE *DI; CODEINE *DI; DEXTROPROPOXYPHENE *DI;
SUPRENORPHINE *DM; CODEINE *DM; DEXTROPROPOXYPHENE *DM;
SUPRENORPHINE *PH; CODEINE *PH; DEXTROPROPOXYPHENE *PH;
SUPRENORPHINE *AR; CODEINE *AR; DEXTROPROPOXYPHENE *AR;
DEXTROMORAMIDE *TR; FENTANYL *TR;
DEXTROMORAMIDE *TR; MORPHINE *TR;
HYDROMORPHONE *AR; MORPHINE *PH;
DEXTROMORAMIDE *DM; FENTANYL *DM;
HYDROMORPHONE *DM; MORPHINE *AR;
DEXTROMORAMIDE *DI; FENTANYL *AR;
HYDROMORPHONE *DI; MORPHINE *DM;
DEXTROMORAMIDE *AR; FENTANYL *DI;
HYDROMORPHONE *PH; MORPHINE *DI;
LEVOMETHADONE *TR; LEVOMETHADONE *DM; LEVOMETHADONE *AR;
LEVOMETHADONE *DI; TR *FT; PH *FT; AR *FT; DM *FT; DI *FT
[06] FENOPROFEN *AR; FLUFENAMATE *AR; FLURBIPROFEN *AR;
INDOMETACIN *AR; KETOPROFEN *AR; NAPROXEN *AR; NIFENAZONE
*AR; NIFLUMATE *AR; OXYPHENBUTAZONE *AR; PHENYLBUTAZONE *AR;
PIROXICAM *AR; TOLMETIN *AR; IRON-SALT *DI; HEPARIN *DI;
CUMARIN *DI; PROBENECID *DI; SULFINPYRAZONE *DI; ACLOFENAC
*AR; AMINOPHENAZONE *AR; LACTYLPHENETIDINE *TR;
LACTYLPHENETIDINE *DM; LACTYLPHENETIDINE *PH;
LACTYLPHENETIDINE *DI; LACTYLPHENETIDINE *DM; MTENAMATE *AR;
TR *FT; AR *FT; PH *FT; DI *FT; DM *FT
FIELD AVAIL.: AR; LA; CT
FILE SEGMENT: Literature

L218 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS ON STM

ACCESSION NUMBER: 2006:1124928 CAPLUS Full-text

DOCUMENT NUMBER: 145:443952

TITLE: Compositions comprising aminergic compounds and

complement compounds, such as ascorbates, cysteines,

opioids, resveratrols, and polycarboxylic acid

chelators

INVENTOR(S): Dillon, Patrick F.; Root-Bernstein, Robert S.

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2006113485 A2 20061026 WO 2006-US14165 20060414
M: AR, AO, AL, AU, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SN, SY, TJ, TM, TN, TR, TT, UA, UG, UZ, VC,
VN, YU, ZA, ZM, ZW
RM: AT, BE, BO, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, CA, GM, GO, GW, ML, MR, NE, SH, TD, TO, BM, GH,
GM, KE, LS, MW, MZ, NA, SD, SE, SZ, TZ, UG, ZM, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2005-672249 P 20050415
US 2005-706249 P 20050805
US 2005-738294 P 20051118
ED Entered STN: 27 Oct 2006
AB Pharmaceutical compns. and method using aminergic compds. and complement
compds. are provided comprising: (a) a subefficacious amount of a non-
adrenergic aminergic compound or of an adrenergic antagonist; and (b) a safe
and effective amount of a complement compound. Methods are also provided
comprising the administration of: (a) a low dose of a non-adrenergic aminergic
compound or any adrenergic antagonist; and (b) a safe and effective amount of
a complement compound. Non-adrenergic aminergic compds. can comprise a
histaminergic, dopaminergic, muscarinic, serotonergic, octopaminergic, or
trace aminergic compound. Complement compds. include ascorbates, opioids,
polycarboxylic acid chelators, resveratrols, cysteines, substituted deriva-
tives and analogs thereof, and mixtures thereof. Preferred complements include
ascorbates, particularly ascorbic acid. Methods include the treatment of
neural and nervous disorders; mood and behavior disorders; cardiac, vascular,
and cardiovascular disorders; hypertension, headache; respiratory disorders;
gastrointestinal disorders; obesity; asthma, allergy; smooth muscle
contraction disorders; nasal or nasopharyngeal conditions; genitourinary
disorders; ocular disorders, glaucoma; and hormone- or neurotransmitter-
release or -secretion disorders.
IT Bronchi, disease
Inflammation
(bronchitis; compns. comprising aminergic compound and
complement compound for treatment of various disorders)
IT Lung, disease
(chronic obstructive pulmonary disease;
compns. comprising aminergic compound and complement compound for treatment
of various disorders)
IT 5-HT agonists
5-HT antagonists
Allergy
Alzheimer's disease
Anticholinergics
Asthma
Bladder, disease

Blood vessel, disease
Cardiovascular system, disease
Chelating agents
Combination chemotherapy
Common cold
Digestive tract, disease
Dopamine agonists
Dopamine antagonists
Emphysema
Epilepsy
Eye, disease
Glaucoma (disease)
Headache
Heart, disease
Human
Hypertension
Influenza
Mental and behavioral disorders
Motion sickness
Mouth, disease
Movement disorders
Muscarinic agonists
Muscarinic antagonists
Nervous system, disease
Nose, disease
Obesity
Parkinson's disease
Prostate gland, disease
Respiratory system, disease
Salivary gland, disease
Schizophrenia
Sexual disorders
Sleep disorders
Urticaria
Vasodilation
Vasoconstriction
α-Adrenoceptor antagonists
β-Adrenoceptor antagonists
(compns. comprising aminergic compound and complement compound for
treatment of various disorders)
IT Drug interactions
(synergistic; compns. comprising aminergic compound and complement compound
for treatment of various disorders)
IT 50-53-3, biological studies 50-55-5, Reserpine 50-60-2, Phentolamine
50-67-9D, 5-Hydroxytryptamine, derivs. 50-81-7D, Ascorbic acid, analogs
and derivs. 51-34-3, Scopolamine 51-45-6D, Histamine, derivs.
51-55-8, Atropine, biological studies 52-86-8, Haloperidol 52-90-4,
L-Cysteine, biological studies 52-90-4D, L-Cysteine, N-(C1-18) acyl
derivs. 54-80-8, Promethazine 55-65-2, Guanethidine 57-27-2,
Morphine, biological studies 57-42-1, Mepredine 58-00-4, Apomorphine
58-73-1, Diphenhydramine 59-96-1, Phenoxymethamine 59-98-3, Tolazoline
60-00-4, EDTA, biological studies 63-75-2, Aprocaine 69-23-8,
Fluphenazine 70-22-4, Oxotremorine 76-41-5, Oxymorphone
76-42-6, Oxycodone 76-57-3, Codeine 76-99-3, Methadone
77-07-6, Levorphanol 82-88-6D, Isyergic acid, derivs. 86-13-5,
Benztropine 82-13-7, Pilocarpine 92-84-2D, Phenothiazine, derivs.
93-65-2, 2-(2-Methyl-4-chlorophenoxy)propanoic acid 107-35-7, Taurine
107-15-7D, Taurine, N-(C1-18) acyl, derivs. 110-89-4D, Piperidine,
diphenylbutyl derivative 113-15-5, Ergotamine 125-28-0, Dihydrocodeine
125-29-1, Hydrocodone 125-71-3, Dextromethorphan 129-03-3,

Cyproheptadine 134-03-2, Sodium ascorbate 146-48-5, Yohimbine
155-58-8, Rhapontin 261-31-4D, Thioxanthene, derivs. 300-62-9,
Amphetamine 359-83-1, Pentastocine 361-37-5, 364-62-5, 437-38-7,
Pentanyol 458-24-2, Fenfluramine 465-65-6, Minoxidil 466-99-9,
Hydrocortisone 469-62-5, Propoxyphene 483-04-5, Rauasine 483-10-3,
Corynanthine 486-12-4, Triprolidine 490-83-5, Dehydroascorbic acid
500-65-2, Rhapontigenin 501-36-0, Resveratrol 511-12-6,
Dihydroergotamine 525-66-6, Propranolol 537-42-8, Pterostilbene
561-27-3, Heroin 575-19-9, 749-02-0, Epiperone 827-61-2, Aceclidine
915-30-0, Diphenoxylate 1477-40-3, Levomethadyl acetate 1977-10-2,
Loxapine 2706-56-1, 2-(2-Pyridyl)ethylamine 2709-56-0, Flupentixol
2933-94-0, Toliprolol 3239-44-9, Dexfenfluramine 3576-73-6,
2-Ethyl-8-methyl-2,8-diazaspiro[5.5]undecane-1,3-dione 3930-20-9, Sotalol
5741-22-0, Meprolol 5743-27-1, Calcium ascorbate 5786-21-0, Clozapine
6452-71-7, Oxprenolol 6673-35-4, Practolol 7413-36-7, Nifedipine
7433-10-5, Butidrine 8006-25-5, Ergotamine 10083-24-6, Piceatanolol
11032-41-0, Dihydroergotamine 13523-86-9, Pindolol 13655-52-2,
Alprenolol 14556-46-8, Bupranolol 15676-16-1, Sulpiride 17479-19-5,
Dihydroergocristine 17692-51-2, Metergoline 18016-80-3, Lisuride
19216-56-9, Prazosin 20229-30-5, Methiothepin 20594-83-6, Halbuphine
21489-74-7, 2-Amino-5,6-dihydroxy-1,2,3,4-tetrahydronaphthalene
23210-56-2, Ifenprodil 23694-81-7, Mepindolol 24219-97-4, Mianserin
25447-65-0, Dihydroergocornine 25447-66-9, Dihydroergocryptine
25523-97-1, Dexchlorpheniramine 25614-03-3, Bromocriptine 26839-75-8,
Timolol 26844-12-2, Indoramine 27848-84-6, Nicergoline 28797-61-7,
Pirnzepine 29122-68-7, Atenolol 29884-49-9, Astrinidin 30187-90-7,
Xibenolol 34661-75-1, Ursipidil 34915-68-9, Bunitrolol 34919-98-7,
Cetamolol 35795-16-5, Trimazolin 36505-84-7, Buspirone 36894-69-6,
Labetalol 37517-30-9, Acebutolol 38163-40-5, Penbutolol 39552-01-7,
Befunolol 39563-28-5, Clonidine 40580-59-4, Quandelal 42200-33-9,
Nadolol 42408-82-2, Butorphanol 42438-89-1, Pinostilbene 47141-42-4,
Levonulolol 50679-08-8, Terfenadine 51384-51-1, Metoprolol
51481-61-9, Cimetidine 51781-06-7, Carteolol 52485-79-7, Buprenorphine
53179-11-6, Loperamide 53648-55-8, Desocine 53684-49-4, Bufetolol
54063-51-3, Nadoxolol 54063-51-3, Propafenone 54340-58-8, Meptazinol
54340-62-4, Bufuralol 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine
55096-26-9, Nalmefene 55273-05-7, Imipromidine 55437-25-7, Bufloxidil
56030-54-7, 56290-94-9, Medroxoalol 56980-93-9, Celiprolol
57149-07-2, Metoprolol 57468-07-0, Talinolol 57536-86-4, 57775-29-8,
Carazolol 57808-66-9, Domperidone 58409-59-9, Bucumolol 58569-55-4,
Met-enkephalin 58822-25-6, Leu-enkephalin 58930-32-8, Butofolol
59170-23-9, Bevantolol 60607-68-3, Indenolol 61869-08-7, Paroxetine
62658-63-3, Bopindolol 63590-64-7, Terazosin 63659-18-7, Betaxolol
64795-35-3, Pseudoergine 65119-89-3, Dimaprit 66104-22-1, Pergolide
66264-77-5, Sulfinalol 66357-35-5, Ranitidine 66722-44-9, Bioprolol
67227-56-9, Fenoldopam 68377-92-4, Arotinolol 69011-14-8, Tiotidine
69906-85-0, Cyanopindolol 70994-56-3, Kyotrophin 71119-11-4,
Bucindolol 71195-58-9, Alfentanil 72822-12-9, Desiprazole
72956-09-3, Carvedilol 74050-98-9, Ketanserin 74135-04-9, Morphine
74191-85-8, Dexazosin 75659-07-3, Dilevalol 78950-78-4, 79617-96-2,
Sertraline 79944-58-4, Idazoxan 80373-22-4, Quinpirole 80755-51-7,
Bunazosin 80880-90-6, Telentapine 81098-60-4, Cilepripide 81147-92-4,
Emmolol 81403-80-5, Alfuzosin 81447-80-5, Dipriferone 81486-22-8,
Nipradilol 81801-12-9, Xanoterol 82855-09-2, Combretastatin
83166-66-9, Nefazodone 83688-84-0, Tertatolol 83928-76-1, Epiprone
85006-82-2, Dynorphin B 85136-71-6, Tiliolol 85320-68-9, Acetazolol
85550-52-8, Mirtazapine 86261-55-9, Onatol 86880-51-5, Spanolol
87051-43-2, Ritanserin 88161-22-2, Dynorphin A 89565-64-4, Tropisetron
98234-03-4, Eltopazine 98233-83-2, Carmoxirole 99614-02-5,
Ondansetron 102203-18-9, Ismetil 103620-46-2, Sumatriptan

AB Title compds. I R1-4 independently = H, alkyl., alkoxy, etc.; R5 and R6 independently = H, alkyl or taken together with the carbon atom to which they are attached to form a 3-8-membered carbocyclic or heterocyclic ring; each R7 and R8 independently = H, alkyl, halo, etc.; J = N or (un)substituted C, provided that no more than two of A, B, D, E and J are N; A, B, D and E independently = N or (un)substituted C; G = alkyl, aryl, aryl, etc.; W = bond, O, S, CH₂, etc.; M = bond, O, CH₂CH₂, etc.; R independently = 1-5, and these pharmacological effects were prepared and disclosed as cannabinoid receptor ligands. Thus, e.g., II was prepared by Suzuki coupling of 2-aminophenylboronic acid with resin bound bromophenol derivative (preparation described). Tested compds. were found to bind to human CB1 and/or CB2 receptor with affinity ranging from 0.1-5000 nM. Further, pharmaceutical compns. containing these compds., and methods for their pharmaceutical use are disclosed. In certain embodiments, the compds. are agonists and/or ligands of cannabinoid receptors and may be useful, inter alia, for treating and/or preventing pain, gastrointestinal disorders, glaucoma, anxiety disorders, inflammation, immunosuppression, autoimmune diseases, ischemic conditions, immune-related disorders, and neurodegenerative diseases, for providing cardioprotection against ischemic and reperfusion effects, for inducing apoptosis in malignant cells, and as an appetite stimulant.

```

IT      Bronchi, disease
        Inflammation
            (bronchitis; preparation of biphenyl derivs. and analogs thereof
            as cannabinoid receptor ligands)
IT      Lung, disease
            (chronic obstructive pulmonary disease;
            preparation of biphenyl derivs. and analogs thereof as cannabinoid receptor
            ligands)
IT      Allergy
        Allergy inhibitors
        Alzheimer's disease
        Analgesics
        Anti-Alzheimer's agents
        Anti-ischemic agents
        Antiarrhythmics
        Antiasthmatics
        Antidiabetic agents
        Antidiarrheals
        Antiemetics
        Antiglaucoma agents
        Antihypertensives
        Antiparkinsonian agents
        Antirheumatic agents
        Appetite stimulants
        Asthma
        Autoimmune disease

```

45

46

10/661458

MO 2005123193	A2	20051229	MO 2005-DK404	20050617
MO 2005123193	A3	20060302		
M: AS, AG, AL, AM, AT, AU, AZ, BA, BB, BO, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HW, IL, IN, IS, JP, KE, KG, KH, KR, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MH, MK, MN, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KO, KZ, MD, RU, TJ, TM, AT, BE, BO, BR, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, ML, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006112274	A1	20060608	US 2005-269289	20051107
MO 2006089546	A1	20060831	MO 2005-DK710	20051107
M: AS, AG, AL, AM, AT, AU, AZ, BA, AB, BO, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, MD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, CY, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:				
			DK 2004-950	A 20040617
			DK 2003-691	A 20030507
			DK 2003-932	A 20030620
			DK 2003-1820	A 20031209
			US 2005-528843P	P 20031209
			MO 2004-DK326	A2 20040506
			MO 2005-DK151	A2 20050228
			MO 2005-DK401	A2 20050617
			MO 2005-DK404	A2 20050617

47

48

100 mg, corn starch (for mixing) 15 mg, corn starch (for paste) 15 mg, and magnesium stearate 10 mg.

IT Analgesic agents
Antiinflammatory agents
Antirheumatic agents
Arthritis
Behcet's syndrome
Cholinergic agonists
Combination chemotherapy
Gout
Human
Osteoarthritis
Pain
Rheumatoid arthritis
Sarcoidosis
Selective estrogen receptor modulators
Tranquilizers
(oral combination of strontium salt and other agents for improvement in treatment of arthritic diseases and associated pain)

IT Drug delivery systems
(oral; oral combination of strontium salt and other agents for improvement in treatment of arthritic diseases and associated pain)

IT Drug delivery systems
(tablets; oral combination of strontium salt and other agents for improvement in treatment of arthritic diseases and associated pain)

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-33-7, Hydrocortisone 50-24-8, Prednisolone 50-33-9, Phenylbutazone, biological studies 50-78-2, Aspirin 52-67-5, Penicillamine 53-03-2, Prednisone 53-06-5, Cortisone 53-86-0, Indomethacin 56-53-1, 57-27-2, Morphine, biological studies 57-42-1, Meperidine 58-15-1, Aminopyrine 59-05-2, Methotrexate 60-80-0, Antipyrine 61-68-7, Mefenamic acid 62-44-2, Phenacetin 62-75-9, Dimethylnitrosamine 64-85-7, Deoxycortone 67-98-1, Ethamoxitriphenol 69-72-7D, Salicylic acid, deriva. 76-42-8, Oxycodone 76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-17-8, Normeperidine 83-41-2, Hydroxychloroquine 124-94-7, Triamcinolone 125-29-1, Hydrocortisone 127-31-0, Fludrocortisone 129-20-4, Oxphenbutazone 147-93-3, Thioalicylic acid 359-83-1, Pentazocine 378-44-9, Betamethasone 437-38-7, Fentanyl 446-72-0, Genistein 446-86-6, Azathioprine 456-99-9, Hydromorphone 493-08-3D, Chroman, deriva. 526-26-1, Strontium salicylate 530-78-9, Flufenacin acid 552-94-3, Salicylate 553-39-9, Allenolic acid 561-27-3, Heroin 564-25-0, Doxycycline 569-57-3, Chlorzoxazone 644-62-2 853-34-9, Rebuzone 868-19-9, Strontium tartrate 911-45-5, Clomiphene 1400-61-9, Nystatin 1845-11-0, Nefopidine 2624-43-3, Cyclophenyl 2809-21-4 3416-24-8, Glucosamine 4419-39-0, Beclomethasone 5104-49-4, Flurbiprofen 5630-53-5, Tibolone 9002-64-6, Parathyroid hormone 9002-72-6, Growth hormone 9004-61-9, Hyaluronic acid 9007-28-7, Chondroitin sulfate 10110-90-8, Minocycline 10448-84-7, Nitrofurantoin 10540-29-1, Tamoxifen 10596-23-3, Clodronate 12244-57-4 13598-36-2D, Phosphoric acid, alkylidenes 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 15721-48-2, Olmesartan 16067-69-9 16088-89-4 20594-83-6, Nalbuphine 21256-18-8, Oxapropion 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22494-42-4, Diflunisal 25322-68-3D, Polyethylene glycol, conjugates with IL-1 receptor deriva. 26173-23-3, Tolmetin 26983-52-8, Diphenol 27203-92-5, Tramadol 27540-07-4 29031-19-4, Glucosamine sulfate 29679-58-1, Fenopropfen 31477-60-8, Ormeloxifene 33369-31-2, Zomepirac 34816-55-2, Moxestrol 36322-90-4.

49

Piroxicam 38194-50-2, Sulindac 40182-75-0, Strontium citrate 40391-99-9 40472-00-2 41340-25-4, Etodolac 41593-31-1, Dihydrochrysen 41839-80-9 42408-62-3, Butorphanol 42924-53-8, Nabumetone 51146-66-6, Desibuprone 51333-22-3, Budesonide 51803-78-2, Wismuth 52485-79-7, Buprenorphine 53587-27-6, Fendosal 53648-55-8, Dexocine 59122-46-2, Mipoprostol 59804-37-4, Tenoxicam 59865-13-3, Cyclosporine 60118-07-2, Endorphin 63524-05-0 66376-36-1, Alendronate 67763-96-6, Insulin-like growth factor-1 68047-06-3, 4-Hydroxytamoxifen 71125-38-7, Meloxicam 74103-06-3, Ketorolac 77599-17-8, Panosifene 78994-23-7, Levormeloxifene 81093-37-0, Pravastatin 82413-20-5, Droloxifene 84449-90-1, Raloxifene 85801-42-9 86111-26-4, Zindoxifene 89750-15-2, Calcitonin-like peptide 2 89778-26-7, Torelifen 89877-06-4, Tiludronate 93957-54-1, Fluvastatin 96007-99-9, ICI 164384 98774-23-3, Temilifen 103735-76-8, erythro-ME 105462-24-6 114084-78-5, Ibendronate 115767-74-3, TAT-59 116057-75-1, Idoxifene 118072-93-8, Zoledronate 121368-58-9, Olpadronate 123663-49-0, T-614 126607-22-7 129453-61-8 129612-87-9, Miproxifene 130996-28-0, P 54 134195-17-8, Cycloextrin sulfate 134523-00-5, Atorvastatin 135459-87-9, Strontium ranelate 137945-48-3, CT 3 138330-18-4, Incadronate 143090-92-0, Anakinra 145599-86-6, Cervastatin 158089-95-3, S-2474 165536-41-4, MDL-103323 169799-44-4, Keratin sulfate 170713-75-4, Nociceptin 175033-36-0, NCK 4016 179469-40-0, strontium derivative 180064-38-4 180916-16-9, Lasofofene 182167-03-9, EM-800 189354-66-3, DFP 190791-29-8, CP-336156 192755-52-5, Prelanacene 194481-32-2, Bazedoxifene 274172-05-7 303730-87-2 322766-10-9, Tirocoxib 507471-54-7 507471-56-9 615258-40-7, AMO 162 630395-06-1, SVT 2016 796104-84-2 796104-86-4 796104-90-0 796842-36-9 796842-37-0 796842-38-1 796842-39-7 796842-40-8 796842-41-5 796842-42-6 796842-43-7 796842-44-8 796842-45-9 796842-46-0 796842-47-1 796842-48-2 796842-49-3 796842-50-4 796842-51-5 796842-52-6 796842-53-7 796842-54-8 796842-55-9 796842-56-0 796842-57-1 796842-58-2 796842-59-3 796842-60-4 796842-61-5 796842-62-6 796842-63-7 796842-64-8 796842-65-9 796842-66-0 796842-67-1 796842-68-2 796842-69-3 796842-70-4 796842-71-5 796842-72-6 796842-73-7 796842-74-8 796842-75-9 796842-76-0 796842-77-1 796842-78-2 796842-79-3 796842-80-4 796842-81-5 796842-82-6 796842-83-7 796842-84-8 796842-85-9 796842-86-0 796842-87-1 796842-88-2 796842-89-3 796842-90-4 796842-91-5 796842-92-6 796842-93-7 796842-94-8 796842-95-9 796842-96-0 796842-97-1 796842-98-2 796842-99-3 796842-100-4 796842-101-5 796842-102-6 796842-103-7 796842-104-8 796842-105-9 796842-106-0 796842-107-1 796842-108-2 796842-109-3 796842-110-4 796842-111-5 796842-112-6 796842-113-7 796842-114-8 796842-115-9 796842-116-0 796842-117-1 796842-118-2 796842-119-3 796842-120-4 796842-121-5 796842-122-6 796842-123-7 796842-124-8 796842-125-9 796842-126-0 796842-127-1 796842-128-2 796842-129-3 796842-130-4 796842-131-5 796842-132-6 796842-133-7 796842-134-8 796842-135-9 796842-136-0 796842-137-1 796842-138-2 796842-139-3 796842-140-4 796842-141-5 796842-142-6 796842-143-7 796842-144-8 796842-145-9 796842-146-0 796842-147-1 796842-148-2 796842-149-3 796842-150-4 796842-151-5 796842-152-6 796842-153-7 796842-154-8 796842-155-9 796842-156-0 796842-157-1 796842-158-2 796842-159-3 796842-160-4 796842-161-5 796842-162-6 796842-163-7 796842-164-8 796842-165-9 796842-166-0 796842-167-1 796842-168-2 796842-169-3 796842-170-4 796842-171-5 796842-172-6 796842-173-7 796842-174-8 796842-175-9 796842-176-0 796842-177-1 796842-178-2 796842-179-3 796842-180-4 796842-181-5 796842-182-6 796842-183-7 796842-184-8 796842-185-9 796842-186-0 796842-187-1 796842-188-2 796842-189-3 796842-190-4 796842-191-5 796842-192-6 796842-193-7 796842-194-8 796842-195-9 796842-196-0 796842-197-1 796842-198-2 796842-199-3 796842-200-4 796842-201-5 796842-202-6 796842-203-7 796842-204-8 796842-205-9 796842-206-0 796842-207-1 796842-208-2 796842-209-3 796842-210-4 796842-211-5 796842-212-6 796842-213-7 796842-214-8 796842-215-9 796842-216-0 796842-217-1 796842-218-2 796842-219-3 796842-220-4 796842-221-5 796842-222-6 796842-223-7 796842-224-8 796842-225-9 796842-226-0 796842-227-1 796842-228-2 796842-229-3 796842-230-4 796842-231-5 796842-232-6 796842-233-7 796842-234-8 796842-235-9 796842-236-0 796842-237-1 796842-238-2 796842-239-3 796842-240-4 796842-241-5 796842-242-6 796842-243-7 796842-244-8 796842-245-9 796842-246-0 796842-247-1 796842-248-2 796842-249-3 796842-250-4 796842-251-5 796842-252-6 796842-253-7 796842-254-8 796842-255-9 796842-256-0 796842-257-1 796842-258-2 796842-259-3 796842-260-4 796842-261-5 796842-262-6 796842-263-7 796842-264-8 796842-265-9 796842-266-0 796842-267-1 796842-268-2 796842-269-3 796842-270-4 796842-271-5 796842-272-6 796842-273-7 796842-274-8 796842-275-9 796842-276-0 796842-277-1 796842-278-2 796842-279-3 796842-280-4 796842-281-5 796842-282-6 796842-283-7 796842-284-8 796842-285-9 796842-286-0 796842-287-1 796842-288-2 796842-289-3 796842-290-4 796842-291-5 796842-292-6 796842-293-7 796842-294-8 796842-295-9 796842-296-0 796842-297-1 796842-298-2 796842-299-3 796842-300-4 796842-301-5 796842-302-6 796842-303-7 796842-304-8 796842-305-9 796842-306-0 796842-307-1 796842-308-2 796842-309-3 796842-310-4 796842-311-5 796842-312-6 796842-313-7 796842-314-8 796842-315-9 796842-316-0 796842-317-1 796842-318-2 796842-319-3 796842-320-4 796842-321-5 796842-322-6 796842-323-7 796842-324-8 796842-325-9 796842-326-0 796842-327-1 796842-328-2 796842-329-3 796842-330-4 796842-331-5 796842-332-6 796842-333-7 796842-334-8 796842-335-9 796842-336-0 796842-337-1 796842-338-2 796842-339-3 796842-340-4 796842-341-5 796842-342-6 796842-343-7 796842-344-8 796842-345-9 796842-346-0 796842-347-1 796842-348-2 796842-349-3 796842-350-4 796842-351-5 796842-352-6 796842-353-7 796842-354-8 796842-355-9 796842-356-0 796842-357-1 796842-358-2 796842-359-3 796842-360-4 796842-361-5 796842-362-6 796842-363-7 796842-364-8 796842-365-9 796842-366-0 796842-367-1 796842-368-2 796842-369-3 796842-370-4 796842-371-5 796842-372-6 796842-373-7 796842-374-8 796842-375-9 796842-376-0 796842-377-1 796842-378-2 796842-379-3 796842-380-4 796842-381-5 796842-382-6 796842-383-7 796842-384-8 796842-385-9 796842-386-0 796842-387-1 796842-388-2 796842-389-3 796842-390-4 796842-391-5 796842-392-6 796842-393-7 796842-394-8 796842-395-9 796842-396-0 796842-397-1 796842-398-2 796842-399-3 796842-400-4 796842-401-5 796842-402-6 796842-403-7 796842-404-8 796842-405-9 796842-406-0 796842-407-1 796842-408-2 796842-409-3 796842-410-4 796842-411-5 796842-412-6 796842-413-7 796842-414-8 796842-415-9 796842-416-0 796842-417-1 796842-418-2 796842-419-3 796842-420-4 796842-421-5 796842-422-6 796842-423-7 796842-424-8 796842-425-9 796842-426-0 796842-427-1 796842-428-2 796842-429-3 796842-430-4 796842-431-5 796842-432-6 796842-433-7 796842-434-8 796842-435-9 796842-436-0 796842-437-1 796842-438-2 796842-439-3 796842-440-4 796842-441-5 796842-442-6 796842-443-7 796842-444-8 796842-445-9 796842-446-0 796842-447-1 796842-448-2 796842-449-3 796842-450-4 796842-451-5 796842-452-6 796842-453-7 796842-454-8 796842-455-9 796842-456-0 796842-457-1 796842-458-2 796842-459-3 796842-460-4 796842-461-5 796842-462-6 796842-463-7 796842-464-8 796842-465-9 796842-466-0 796842-467-1 796842-468-2 796842-469-3 796842-470-4 796842-471-5 796842-472-6 796842-473-7 796842-474-8 796842-475-9 796842-476-0 796842-477-1 796842-478-2 796842-479-3 796842-480-4 796842-481-5 796842-482-6 796842-483-7 796842-484-8 796842-485-9 796842-486-0 796842-487-1 796842-488-2 796842-489-3 796842-490-4 796842-491-5 796842-492-6 796842-493-7 796842-494-8 796842-495-9 796842-496-0 796842-497-1 796842-498-2 796842-499-3 796842-500-4 796842-501-5 796842-502-6 796842-503-7 796842-504-8 796842-505-9 796842-506-0 796842-507-1 796842-508-2 796842-509-3 796842-510-4 796842-511-5 796842-512-6 796842-513-7 796842-514-8 796842-515-9 796842-516-0 796842-517-1 796842-518-2 796842-519-3 796842-520-4 796842-521-5 796842-522-6 796842-523-7 796842-524-8 796842-525-9 796842-526-0 796842-527-1 796842-528-2 796842-529-3 796842-530-4 796842-531-5 796842-532-6 796842-533-7 796842-534-8 796842-535-9 796842-536-0 796842-537-1 796842-538-2 796842-539-3 796842-540-4 796842-541-5 796842-542-6 796842-543-7 796842-544-8 796842-545-9 796842-546-0 796842-547-1 796842-548-2 796842-549-3 796842-550-4 796842-551-5 796842-552-6 796842-553-7 796842-554-8 796842-555-9 796842-556-0 796842-557-1 796842-558-2 796842-559-3 796842-560-4 796842-561-5 796842-562-6 796842-563-7 796842-564-8 796842-565-9 796842-566-0 796842-567-1 796842-568-2 796842-569-3 796842-570-4 796842-571-5 796842-572-6 796842-573-7 796842-574-8 796842-575-9 796842-576-0 796842-577-1 796842-578-2 796842-579-3 796842-580-4 796842-581-5 796842-582-6 796842-583-7 796842-584-8 796842-585-9 796842-586-0 796842-587-1 796842-588-2 796842-589-3 796842-590-4 796842-591-5 796842-592-6 796842-593-7 796842-594-8 796842-595-9 796842-596-0 796842-597-1 796842-598-2 796842-599-3 796842-600-4 796842-601-5 796842-602-6 796842-603-7 796842-604-8 796842-605-9 796842-606-0 796842-607-1 796842-608-2 796842-609-3 796842-610-4 796842-611-5 796842-612-6 796842-613-7 796842-614-8 796842-615-9 796842-616-0 796842-617-1 796842-618-2 796842-619-3 796842-620-4 796842-621-5 796842-622-6 796842-623-7 796842-624-8 796842-625-9 796842-626-0 796842-627-1 796842-628-2 796842-629-3 796842-630-4 796842-631-5 796842-632-6 796842-633-7 796842-634-8 796842-635-9 796842-636-0 796842-637-1 796842-638-2 796842-639-3 796842-640-4 796842-641-5 796842-642-6 796842-643-7 796842-644-8 796842-645-9 796842-646-0 796842-647-1 796842-648-2 796842-649-3 796842-650-4 796842-651-5 796842-652-6 796842-653-7 796842-654-8 796842-655-9 796842-656-0 796842-657-1 796842-658-2 796842-659-3 796842-660-4 796842-661-5 796842-662-6 796842-663-7 796842-664-8 796842-665-9 796842-666-0 796842-667-1 796842-668-2 796842-669-3 796842-670-4 796842-671-5 796842-672-6 796842-673-7 796842-674-8 796842-675-9 796842-676-0 796842-677-1 796842-678-2 796842-679-3 796842-680-4 796842-681-5 796842-682-6 796842-683-7 796842-684-8 796842-685-9 796842-686-0 796842-687-1 796842-688-2 796842-689-3 796842-690-4 796842-691-5 796842-692-6 796842-693-7 796842-694-8 796842-695-9 796842-696-0 796842-697-1 796842-698-2 796842-699-3 796842-700-4 796842-701-5 796842-702-6 796842-703-7 796842-704-8 796842-705-9 796842-706-0 796842-707-1 796842-708-2 796842-709-3 796842-710-4 796842-711-5 796842-712-6 796842-713-7 796842-714-8 796842-715-9 796842-716-0 796842-717-1 796842-718-2 796842-719-3 796842-720-4 796842-721-5 796842-722-6 796842-723-7 796842-724-8 796842-725-9 796842-726-0 796842-727-1 796842-728-2 796842-729-3 796842-730-4 796842-731-5 796842-732-6 796842-733-7 796842-734-8 796842-735-9 796842-736-0 796842-737-1 796842-738-2 796842-739-3 796842-740-4 796842-741-5 796842-742-6 796842-743-7 796842-744-8 796842-745-9 796842-746-0 796842-747-1 796842-748-2 796842-749-3 796842-750-4 796842-751-5 796842-752-6 796842-753-7 796842-754-8 796842-755-9 796842-756-0 796842-757-1 796842-758-2 796842-759-3 796842-760-4 796842-761-5 796842-762-6 796842-763-7 796842-764

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005222136	A1	20051006	US 2004-987803	20041112
CA 2562219	AA	20051020	CA 2005-2562219	20050405
WO 2005097099	A1	20051020	WO 2005-EP3641	20050405

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GO, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: ES 2004-4000844 A 20040405
ES 2004-844 A 20040405
US 2004-987803 A 20041112
WO 2005-EP3641 W 20050405

OTHER SOURCE(S): MARPAT 143:373377

ED Entered STM: 07 Oct 2005

AB The present invention relates to an active substance combination including at least one substituted carbinol compound and at least one non-steroidal anti-inflammatory drug (NSAID), a medicament including the active substance combination, a pharmaceutical formulation including the active substance combination and the use of the active substance combination for the manufacture of a medicament.

TI Pharmaceutical active substance combination comprising substituted carbinol compounds and non-steroidal anti-inflammatory drugs

ST pharmaceutical combination substituted carbinol compd nonsteroidal antiinflammatory drug

IT Urogenital system
(-related pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation
(Crohn's disease; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Intestine, disease
(Crohn's; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal
(Hodkin's disease; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal
(Peutz-Jegher syndrome; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal
(Isleterodoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drugs of abuse
(abuse of, treatment and prevention of; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

53

IT Pain
(acute; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma
(adenocarcinoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Swelling, biological
(after injury; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Transplant and Transplantation
(allotransplant, cornea, rejection; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Heart, disease
(angina pectoris, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Blood vessel, neoplasm
(angioblastoma, nasopharynx; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation
Spinal column, disease
(ankylosing spondylitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Anemia (disease)
(aplastic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal
(arthropathy, Bursitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal
(back pain, lower, chronic pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Body, anatomical
(back, disease, pain, lower, chronic pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain
(back, lower, chronic pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Skin, neoplasm
(basal cell carcinoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma
(basal cell; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Injury
(bone, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

54

non-steroidal anti-inflammatory drugs)

IT Bronchi, disease
Inflammation
(bronchitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Epithelium
(cancer effecting; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Lip
(cancer; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(capsules; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Ischemia
(cardiac; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain
(central, post-operative; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Uterus, neoplasm
(cervix, carcinoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma
(cervix; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain
(chronic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Headache
(cluster; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Intestine, neoplasm
(colon; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye, disease
Inflammation
(conjunctivitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye
(cornea, allotransplant, rejection; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Transplant rejection
(corneal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Bladder, disease

55

Inflammation
(cystitis, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain
(dental; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Mental and behavioral disorders
(depression; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye, disease
(diabetic retinopathy; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Joint, anatomical
(disease, Bursitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Viscera
(disease, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Joint, anatomical
(disease, sprain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Tendon
(disease, tendinitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(dragees; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(drops; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Uterus, disease
(endometriosis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(enteric-coated; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Alcohol, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fatty; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Ulcer
(gastric; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation
Stomach, disease
(gastritis; pharmaceutical active substance

56

combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(gels; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Gingiva, disease
Inflammation
(gingivitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(granules; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Bladder, disease
(incontinence; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal
(infantile hemangiomas; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Intestine, disease
(inflammatory; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(injections, i.m.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(injections, i.p.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(injections, i.v.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(injections, s.c.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Bone, disease
(injury, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Autoimmune disease
(insulin-dependent diabetes mellitus; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Diabetes mellitus
(insulin-dependent; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(intrathecal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Intestine, disease

(irritable bowel syndrome; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Heart, disease
(ischemia; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Rheumatoid arthritis
(juvenile; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(liq.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Angiogenesis
(mediated disorder; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Neoplasm
(metastasis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Hydrocarbon waxes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Headache
(migraine; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(mucosal, transmucosal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(nasal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pharynx
(nasopharynx, angiofibroma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Glaucoma (disease)
(neovascular; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Angiogenesis
(neovascularization, eye; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye, disease
(neovascularization; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Kidney, disease
(nephrotic syndrome; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Nerve, disease
Pain
(neuralgia, Herpes; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation
(neurogenic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Nerve, disease
(neuropathy, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Nerve
(nociceptive, pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Anti-inflammatory agents
(nonsteroidal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(oral; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Burn
Head and Neck
Furunculosis
Sunburn
Surgery
Tooth, disease
(pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(parenteral; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(pellets; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Artery, disease
Inflammation
(periarthritis nodosa; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Arm
Leg
(phantom limb pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Analgesics
Anti-infective agents
Anti-inflammatory agents
Antiarthritics
Antiaesthetics
Antidepressants
Antidiabetic agents
Antirheumatic agents

Antitumor agents
Antiulcer agents
Antiviral agents
Arthritis
Asthma
Beeswax
Behcet's syndrome
Bladder, neoplasm
Blood vessel, disease
Bone, neoplasm
Brain, neoplasm
Carcinoma
Common cold
Dermatitis
Digestive tract, disease
Digestive tract, neoplasm
Dysmenorrhea
Eczema
Edema
Fever and Hyperthermia
Gelation agents
Gout
Headache
Inflammation
Influenza
Liver, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Myasthenia gravis
Myositis
Neoplasm
Opioid antagonists
Osteoarthritis
Ovary, neoplasm
Pancreas, neoplasm
Plasticizers
Prostate gland, neoplasm
Psoriasis
Rheumatic fever
Rheumatoid arthritis
Sarcoidosis
Skin, disease
Skin, neoplasm
Strain
(pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carnuba wax
Fats and Glyceric oils, biological studies
Fatty acids, biological studies
Opioids
Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Myositis
(polymyositis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(rectal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Kidney, neoplasm
(renal cell carcinoma; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma
(renal cell; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye
(retina, neovascularisation; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Eye, disease
(retrolental fibroplasia; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(orals; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Spinal column, disease
(spondyloarthropathy; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal
(sprain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Carcinoma
(squamous cell; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(suspensions; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(sustained-release; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Injury
(swelling; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Arthritis
Synovial membrane, disease
(synovitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(syrups; pharmaceutical active substance combination

comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Lupus erythematosus
(systemic; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(tablets, immediate release; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(tablets; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation
(tendinitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation
Thyroid gland, disease
(thyroiditis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Drug delivery systems
(transdermal; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Stomach, disease
(ulcer; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Inflammation
Intestine, disease
(ulcerative colitis; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Bone, disease
(vascular necrosis of bone; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Infection
(viral; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Disease, animal
(visceral pain; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT Pain
(visceral; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT 561-27.3, Diacetylmorphine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heroin; pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT 50-33.9, Phenylbutazone, biological studies 50-78.2, Acetylsalicylic acid 53-86.1, Indomethacin 56-81.5, 1,2,3-Propanetriol, biological studies 57-27.2, Morphine, biological studies 57-42.1.

Pethidine 61-68-7, Mefenamic acid 62-67-9, Nalorphine 65-45-2, Salicylamide 67-56-1, Carbinol, biological studies 68-89-3, Metamizol 71-50-1, Acetate, biological studies 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 76-58-4, Ethylmorphine 77-07-6, Levorphanol 92-43-3, Phenidone 103-90-2, Paracetamol 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 125-58-6, Levomethadone 129-20-4, Oxypentazone 152-02-3, Levallorphan 288-13-1, Pyrazole 288-32-4, Imidazole, biological studies 302-41-0, Pirritramide 357-56-2, Dextromoramide 359-83-1, Pentazocine 437-38-7, Fentanyl 465-65-6, Meloxone 466-99-9, Hydroxymorphone 469-62-5, Dextropropoxyphene 469-79-4, Ketobemidone 479-92-5, Propoxyphazone 530-78-9, Flufenamic acid 644-62-2, Meclofenamic acid 653-34-9, Kebuzone 915-10-0, Diphenoxylate 938-73-8, Ethenzamide 1477-40-3, Levomethadyl 2210-63-1, Mefebutazone 2438-72-4, Bufexamac 4394-00-7, Niflumic acid 5104-49-4, Flurbiprofen 9004-34-6D, Cellulose, ester 9004-57-3, Ethyl cellulose 14521-96-3, Etorphine 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16590-41-3, Maltrexone 20594-03-6, Nalbuphine 21256-18-8, Oxapropzin 21363-18-8, Viminal 22071-64-8, Ketoprofen 22204-53-1, Naproxen 22494-42-4, Diflunisal 24171-33-3, Tolmetin 27201-92-5, Tramadol 29679-58-1, Fenpropfen 30231-64-8, Glycerol monobenhenate 30544-47-9, Etofenamate 30748-29-9, Feprazone 31566-31-1, Glycerol monostearate 33005-95-7, Tiaprofenic acid 34552-84-6, Isoxicam 36322-90-4, Piroxicam 36330-85-5, Fenbufen 38194-50-2, Sulindac 41340-25-4, Etodolac 42408-82-2, Butorphanol 42924-53-8, Nabumetone 51803-78-2, Nimesulide 51931-66-9, Tilidine 52485-79-7, Buprenorphine 53164-05-9, Acemetacin 53179-11-6, Loperamide 53648-55-8, Desocine 53808-88-1, Lonazolac 54340-58-8, Meptazinol 56030-54-7, Butantanil 59804-37-4, Tenoxicam 66532-85-2, Propacetamol 70374-39-9, Lornoxicam 71125-38-7, Meloxicam 71195-59-9, Alfentanil 74103-06-3, Ketorolac 112344-52-2, Plobuten 122154-30-7 122154-31-8 122154-32-9 122154-33-0 122154-35-2 122154-36-3 122154-37-4 122154-38-5 122154-39-6 122154-40-9 122154-41-0 122154-42-1 122154-43-2 122154-44-3 122154-45-4 122154-46-5 122154-47-6 122154-49-8 122154-51-2 122154-52-3 122154-53-4 122154-55-6 122154-56-7 122154-57-8 122154-60-3 122154-63-6 122154-67-0 122154-68-1 122154-69-2 122154-70-5 122154-71-6 122154-72-7 122154-73-8 122154-74-9 122154-75-0 122154-76-1 122154-77-2 122154-78-3 122154-79-4 122154-80-7 122154-81-8 122154-82-9 122154-83-0 122154-84-1 122154-85-2 122154-86-3 122154-87-4 122154-88-5 122154-89-6 122154-90-9 122154-91-0 122154-92-1 122154-93-2 122154-94-3 122154-95-4 122154-96-5 122154-97-6 122154-98-7 122154-99-8 122155-00-4 122155-01-5 122155-02-6 122155-03-7 122155-04-8 122155-06-0 122155-08-2 122155-09-3 122155-10-4 122155-11-5 122155-12-6 122155-13-7 122155-14-8 122155-15-9 122155-16-0 122155-17-0 122155-18-1 122155-19-2 122155-20-3 122155-21-4 122155-22-5 122155-23-6 122155-24-7 122155-25-8 122155-26-9 122155-27-0 122155-28-1 122155-29-2 122155-30-3 122155-31-4 122155-32-5 122155-33-6 122155-34-7 122155-35-8 122155-36-9 122155-37-0 122155-38-1 122155-39-2 122155-40-3 122155-41-4 122155-42-5 122155-43-6 122155-44-7 122155-45-8 122155-46-9 122155-47-0 122155-48-1 122155-49-2 122155-50-3 122155-51-4 122155-52-5 122155-53-6 122155-54-7 122155-55-8 122155-56-9 122155-57-0 122155-58-1 122155-59-2 122155-60-3 122155-61-4 122155-62-5 122155-63-6 122155-64-7 122155-65-8 122155-66-9 122155-67-0 122155-68-1 122155-69-2 122155-70-3 122155-71-4 122155-72-5 122155-73-6 122155-74-7 122155-75-8 122155-76-9 122155-77-0 122155-78-1 122155-79-2 122155-80-3 122155-81-4 122155-82-5 122155-83-6 122155-84-7 122155-85-8 122155-86-9 122155-87-0 122155-88-1 122155-89-2 122155-90-3 122155-91-4 122155-92-5 122155-93-6 122155-94-7 122155-95-8 122155-96-9 122155-97-0 122155-98-1 122155-99-2 122156-00-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

IT 122175-93-3 122175-94-4 122175-95-5 122175-96-6 122175-97-7 122175-98-8 122175-99-9 122176-00-0 122176-01-6 131575-03-6, 14-Methoxymetopon 132875-61-7, Remifentanyl 142155-43-9 148981-63-9 148981-65-1 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 198470-84-7, Parecoxib 202409-33-4, Etoricoxib 247046-52-2 247046-53-3 247046-54-4 247046-55-5 247046-56-6 247046-57-7 247046-58-8 247046-59-9 247046-60-2 247046-61-3 247046-62-4 247046-63-5 247046-64-6 247046-65-7 247046-66-8 247046-67-9 247046-68-0 247046-69-1 247046-70-4 247046-71-5 247046-72-6 258329-52-3 258329-53-4 258329-54-5 258329-55-6 258329-56-7 258329-57-8 258329-58-9 258329-59-0 258329-60-1 258329-61-2 258329-62-3 258329-63-4 258329-64-5 258329-65-6 258329-66-7 258329-67-8 258329-68-9 258329-69-0 258329-70-3 258329-71-4 258329-72-5 258329-73-6 258329-74-7 258329-75-9 258329-76-0 258329-77-1 258329-78-2 866218-44-2 866218-45-3 866218-46-4 866218-47-5 866218-48-6 866218-49-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical active substance combination comprising substituted carbinol compds. and non-steroidal anti-inflammatory drugs)

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005033073	A2	20050814	(200530)	EN	573[0]	
US 20050159438	A1	20050721	(200544)	EN		
EP 1675847	A2	20060705	(200644)	EN		

PATENT NO	KIND	APPLICATION	DATE
WO 2005033073	A2	WO 2004-0532479	20041001
US 20050159438	A1 Provisional	US 2003-5078449	20031001
US 20050159438	A1	US 2004-0507554	20041001
EP 1675847	A2	EP 2004-817130	20041001
EP 1675847	A2	WO 2004-0532479	20041001

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1675847	A2	Based on WO 2005033073 A

PRIORITY APPLN. INFO: US 2003-507864P 20031001
US 2004-957554 20041001

TECH

ORGANIC CHEMISTRY - Preferred Compounds: (I') comprise compounds of formula (I'a).

R1 and R3 = H, alkyl, alkenyl, alkynyl or aryl;
Z = -N(R5)-;
R2 = H, (cyclo)alkyl, alkenyl, alkynyl, alkylcycloalkyl or (hetero)aryl;
R1-R3, R1-R2 and R2-R3 = 4-8-membered heterocycloalkyl ring;
Ra = H or alkyl;
Rb = H, alkyl or aryl;
n = 0-3;
A and B' = H, fluoro or alkyl;
A-B' = a double bond between the carbon atoms to which they are attached;
R4 = -Y-W;
Y = a single bond, C(Ra)(Rb), C(Ra)(Rb)C(Ra)(Rb) or C(Ra)(Rb)C(Ra)(Rb)C(Ra)(Rb);
W = (hetero)aryl;
X = -CH2-, -O-, -S-, -SO-, -SO2 or -N(R5)-;
R5 = H, (cyclo)alkyl, -(CH2)-alkenyl, -(CH2)-alkynyl, aryl, -CORb or -SO2Rb;
J-carbon atoms to which it is attached = 6-membered aryl or 5- or 6-membered heteroaryl ring.
Provided that:
(a) when R2 is other than -CH(C(=O)-ORb)(Ra), then R1-R2 and R2-R3 form 4-8-membered heterocycloalkyl ring; when J taken together with the carbon atoms to which it is attached forms a phenyl optionally mono- to tri-substituted by -S-1-4C alkyl, 1-4C alkyl (both optionally substituted by at least one halo or 1-4C alkoxy); halo or ORb, W is unsubstituted naphthyl or phenyl optionally mono- to tri-substituted by halo, 1-4C alkyl, 1-6C alkoxy, phenyl, phenoxy, 1,3-benzodioxazolyl, 2,2-difluoro-1,3-benzodioxazolyl, HW2, -N(1-4C alkyl)2 or pyrrollyl; n is 1; R1 and R3 are H; A-B forms a double bond between atoms to which they are attached; Y is a single bond; and X is -O-; then R2 is other than H or methyl; when J taken together with the carbon atoms to which it is attached forms a phenyl ring; W is phenyl optionally mono- to tri-substituted by fluoro, ORb, 1-6C alkoxy (optionally substituted by at least one fluoro), 2-6 alkenyloxy or -S-1-4C alkyl; n is 1; R1 and R3 are H; A-B' forms a double bond between atoms to which they are attached; Y is a single bond; and X is -O-; then R2 is other than H or benzyl; and when J forms a 6-membered aryl ring, then it is substituted with other than pyrimidine-2,4-diamine-meth-5-yl.
In (I'), the spiro carbon and/or the carbon to which -Y-W is attached (preferably the carbon to which -Y-W is attached, or the spiro carbon and the carbon to which -Y-W is attached) is chiral. Preparation: (i) can be prepared by 37 methods as given in the specification e.g. preparation of (Ia) (where X is CH or H) involves:
(a) condensing 2'-hydroxyacetophenone derivative of formula (i) with 1-Boc-4-piperidone in pyrrolidone derivative of formula (ii) at room temperature to obtain N-Boc-spiro(2H-1-benzopyran-2,4'-piperidine)-4(3H)-one derivative of formula (iii);
(b) converting (iii) into an enol triflate derivative of formula (v) using

N-phenylbis(trifluoromethanesulfonamide) of formula (iv) as a triflating agent; and
(c) coupling (v) by Suzuki type coupling with 4-(N,N-diethylaminocarbonyl)phenyl boronic acid (vi) in ethylene glycol dimethyl ether in the presence of tetrakis triphenylphosphine palladium(0) (10 wt.%) on activated carbon, lithium chloride and aqueous solution of sodium carbonate to obtain a substituted spiro(2H-1-benzopyran-2,4'-piperidine) compound of formula (viii), followed by conversion under acidic conditions. Ru-Ry = not defined.
PHARMACEUTICALS - Preferred Composition: The composition further comprises an antibiotic, antiviral, antifungal, anti-inflammatory and/or anesthetic. Preferred Drugs: The opioid is selected from 73 drugs(s), or their diastereomers, salts or complexes as given in the specification e.g. allylprodine, dextromoramide, etazocine, fentanyl, ketobesidone, loperamide, lofentanil, myrophine, piritramide, tilidine. The agent for the treatment of neuralgic/neuropathic pain is a mild OTC analgesic, a narcotic analgesic, an antispasmodic medication or an anti-depressant. The agent for the treatment of depression is a selective serotonin re-uptake inhibitor, a tricyclic compound, a monoamine oxidase inhibitor or an antidepressant compound belonging to the heterocyclic class. The agent for the treatment of incontinence is an anticholinergic agent, an antispasmodic medication, a tricyclic antidepressant, a calcium channel blocker or a beta agonist. An agent for the treatment of Parkinson's disease is selected from deprenyl, amantadine, levodopa or carbidopa. Preferred Method: The prevention or treatment of pain with (I) further involves administering an opioid. The prevention or treatment of urogenital tract disorder with (I) further involves administering an agent for the treatment of incontinence. The prevention or treatment of depression with (I) further involves administering an agent for the treatment of depression. The prevention or treatment of tremors with (I) further involves administering an antiparkinsonian agent. The production or maintenance of an anesthetic state with (I) further involves administering an anesthetic agent selected from an inhaled anesthetic, a hypnotic, an anxiolytic, a neuromuscular blocker or an opioid.

L218 ANSWER 17 OF 19 WPJX COPYRIGHT 2006 THE THOMSON CORP on STM
ACCESSION NUMBER: 2006-030913 [04] WPJX
DOC. NO. CFI: C2006-011203 [04]
TITLE: Use of opioid controlled release oral dosage form for treating chronic obstructive pulmonary disease
DERIVAT CLASS: B02
INVENTOR: FLEISCHER W; LEYENDECKER P; REIMER K
PATENT ASSIGNEE: (EURO-H) EUROCELLTQUE SA
COUNTRY COUNT: 110
PATENT INFO ABBR.:
PATENT NO KIND DATE WEEK LA PG MAIN IPC
EP 1604666 A1 20051214 (200604) EN 24 [0]
WO 2005120507 A1 20051222 (200604) EN

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1604666 A1		EP 2004-13468	20040608
WO 2005120507 A1		WO 2005-EP6155	20050608

PRIORITY APPLN. INFO: EP 2004-13468 20040608

TECH

PHARMACEUTICALS - Preferred Dosage: The dosage comprises an opioid agonist (e.g. oxycodone, hydrocodone, hydromorphone, morphine, methadone, oxycodone, fentanyl or sufentanil in the form of free base or salt) or a mixture of opioid agonist and opioid antagonist (e.g. naltrexone, nalbuphine or naloxone in the form of free base or salt). Preferably the dosage comprises oxycodone, morphine or a mixture of oxycodone (10 - 150, preferably 10 - 80 mg) and naloxone (1 - 50 mg). Oxycodone and naloxone are present in a ratio up to 25:1 (preferably up to 20:1, especially 2:1 or 1:1). Preferably amount of oxycodone is higher than that of naloxone. The compounds are released from the dosage in a sustained, invariant or independent manner.

L218 ANSWER 18 OF 19 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STM

ACCESSION NUMBER: 2005081426 EMBASE Full-text
TITLE: Prospective audit of short-term concurrent ketamine, opioid and anti-inflammatory ('triple-agent') therapy for episodes of acute on chronic pain.
AUTHOR: Good P.; Tullio P.; Jackson K.; Goodchild C.; Ashby M.
CORPORATE SOURCE: Prof. M. Ashby, Centre for Palliative Care, St. Vincent's Hospital, University of Melbourne, PO Box 2900, Fitzroy, Vic. 3065, Australia. ashby@unimelb.edu.au
SOURCE: Internal Medicine Journal, (2005) Vol. 35, No. 1, pp. 39-44.
Ref: 33
ISSN: 1444-0903 CODEN: IMJNAX
COUNTRY: Australia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
016 Cancer
017 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STM: 3 Mar 2005
Last Updated on STM: 3 Mar 2005

ABSTRACT: Aim: This prospective audit was undertaken in order to document the analgesic response and adverse effects of concurrent short-term ('burst') triple-agent analgesic (ketamine, an opioid and an anti-inflammatory agent - either steroidal or non-steroidal) administration, for episodes of acute on chronic pain. The clinical hypothesis in this study is that better pain control may be obtained by simultaneous multiple target receptor blockade. Method: The response of 18 patients is reported. The pain and analgesic requirement data for the 24 h before starting triple-agent therapy were compared with the last 24 h on the triple-agent therapy. Patients were then classified as responders or non-responders. Results: According to stringent clinical criteria, 12 out of the 18 patients were classified as responders. The response rate was highest for somatic pain (7/9) and appeared to decrease with duration of prior uncontrolled pain. Only four out of the 18 patients reported adverse effects and all of these were minor. Conclusions: The results suggest that this 'burst' triple-agent approach is safe and effective in an inpatient palliative care population during episodes of poorly controlled acute on chronic pain, and warrants further investigation to ascertain whether it gives superior results compared to the 'gold-standard' WHO ladder approach.

CONTROLLED TERM: Medical Descriptors:
*short course therapy
*cancer pain: CO, complication
*cancer pain: DT, drug therapy
*chronic pain: CO, complication
*chronic pain: DT, drug therapy
*neuropathic pain: CO, complication
*neuropathic pain: DT, drug therapy
*proactive study
*analgesic activity
*receptor blocking
*drug safety
*drug efficacy
*world health organization
*lung cancer
*head and neck cancer
*breast cancer
*skin cancer
*prostate cancer
*kidney cancer
*colorectal cancer
*fragility fracture
*drowsiness: S1, side effect
*confusion: S1, side effect
*hallucination: S1, side effect
*human
*male
*female
*clinical article
*controlled study
*aged
*adult
*article
*priority journal
*Drug Descriptors:
*ketamine: AS, adverse drug reaction
*ketamine: CB, drug combination
*ketamine: DT, drug therapy
*ketamine: IV, intravenous drug administration
*narcotic analgesic agent: AS, adverse drug reaction
*narcotic analgesic agent: CB, drug combination
*narcotic analgesic agent: DT, drug therapy
*narcotic analgesic agent: IV, intravenous drug administration
*antiinflammatory agent: AS, adverse drug reaction
*antiinflammatory agent: CB, drug combination
*antiinflammatory agent: DT, drug therapy
*antiinflammatory agent: IV, intravenous drug administration
*nonsteroid antiinflammatory agent: AS, adverse drug reaction
*nonsteroid antiinflammatory agent: CB, drug combination
*nonsteroid antiinflammatory agent: DT, drug therapy
*nonsteroid antiinflammatory agent: IV, intravenous drug administration
*steroid: AS, adverse drug reaction
*steroid: CB, drug combination
*steroid: DT, drug therapy

steroid: IV, intravenous drug administration
ketorolac: AS, adverse drug reaction
ketorolac: CB, drug combination
ketorolac: DT, drug therapy
ketorolac: IV, intravenous drug administration
naproxen: AS, adverse drug reaction
naproxen: CB, drug combination
naproxen: DT, drug therapy
naproxen: IV, intravenous drug administration
dexamethasone: AS, adverse drug reaction
dexamethasone: CB, drug combination
dexamethasone: DT, drug therapy
dexamethasone: IV, intravenous drug administration
parecoxib: AS, adverse drug reaction
parecoxib: CB, drug combination
parecoxib: DT, drug therapy
parecoxib: IV, intravenous drug administration
morphine: AS, adverse drug reaction
morphine: CB, drug combination
morphine: DO, drug dose
morphine: DT, drug therapy
morphine: IV, intravenous drug administration
hydromorphone: AS, adverse drug reaction
hydromorphone: CB, drug combination
hydromorphone: DO, drug dose
hydromorphone: DT, drug therapy
hydromorphone: IV, intravenous drug administration
oxycodone: AS, adverse drug reaction
oxycodone: CB, drug combination
oxycodone: DO, drug dose
oxycodone: DT, drug therapy
oxycodone: IV, intravenous drug administration
prednisolone: AS, adverse drug reaction
prednisolone: CB, drug combination
prednisolone: DO, drug dose
prednisolone: DT, drug therapy
(ketamine) 1847-66-9, 6740-88-1, 81771-21-3; (ketorolac)
74101-06-3; (naproxen) 22204-53-1, 24159-34-2;
(dexamethasone) 50-02-2; (parecoxib) 198470-84-7,
198470-85-8; (morphine) 52-26-6, 57-27-2; (hydromorphone)
466-99-9, 71-68-1; (oxycodone) 124-90-3, 76-42-6;
(prednisolone) 50-24-8

CAS REGISTRY NO.:

L218 ANSWER 19 OF 19 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2000116057 EMBASE Full-text

TITLE: Managing addiction in advanced cancer patients: Why Bother?

AUTHOR: Passik S.D.; Theobald D.S.

CORPORATE SOURCE: Dr. S.D. Passik, Community Cancer Care Inc., 115 West 19th Street, Indianapolis, IN 46202, United States

SOURCE: Journal of Pain and Symptom Management, (2000) Vol. 19, No. 3, pp. 229-234.

Refs: 8
ISSN: 0885-3924 CODEN: JPSMKU
S 0885-3924(00)00109-3

PUBLISHER IDENT.: United States

COUNTRY: Journal, Article

DOCUMENT TYPE: 016 Cancer

FILE SEGMENT: 032 Psychiatry

69

036 Health Policy, Economics and Management
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
008 Neurology and Neurosurgery

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Apr 2000
Last Updated on STN: 13 Apr 2000

ABSTRACT: The management of addiction in patients with advanced cancer can be time-consuming, labor-intensive, and difficult. Some clinicians believe that it is not worth the effort, due in part to a failure to appreciate the deleterious impact of addiction on palliative care efforts and a view of addiction as intractable in any case. Indeed, it is possible that some clinicians perceive addiction not only fatalistically but, because of common misconceptions, believe that managing or attempting to decrease the patient's use of alcohol or illicit substances would be tantamount to depriving a dying patient of a source of pleasure. In this paper, we argue that managing addiction is an essential aspect of palliative care for chemically-dependent and alcoholic patients. The goal of such efforts is not complete abstinence, but exerting enough control over illicit drug and alcohol use to allow palliative care interventions to decrease suffering. To illustrate this view, we describe two patients with chemical dependency. We highlight the impact of unchecked substance abuse on patient's perpetuation of their own suffering, the complication of symptom management, the diagnosis and treatment of mood/anxiety disorders, and the effect on the patients' family and caregivers. Copyright (c) 2000 U.S. Cancer Pain Relief Committee.

CONTROLLED TERM: Medical Descriptors:
*addiction
*cancer patient
palliative therapy
drug abuse
anxiety neurosis: ET, etiology
anxiety neurosis: DT, drug therapy
anxiety neurosis: CO, complication
smoking
advanced cancer
alcoholism: TH, therapy
group therapy
adenocarcinoma
pleura metastasis: SU, surgery
pleura effusion: TH, therapy
drain
withdrawal syndrome: PC, prevention
withdrawal syndrome: DT, drug therapy
cancer pain: DT, drug therapy
cancer pain: CO, complication
patient information
caregiver
insomnia: DT, drug therapy
insomnia: CO, complication
heroin dependence
lung cancer: RT, radiotherapy
human
male
case report
adult
article
Drug Descriptors:
alcohol

70

10/661458

illicit drug
lorazepam: DT, drug therapy
lorazepam: CB, drug combination
oxycodone: DT, drug therapy
oxycodone: CB, drug combination
paracetamol: DT, drug therapy
paracetamol: CB, drug combination
trazodone: DT, drug therapy
trazodone: CB, drug combination
fentanyl: DT, drug therapy
fentanyl: CB, drug combination
fentanyl: TD, transdermal drug administration
fentanyl: IV, intravenous drug administration
(alcohol) 64-17-5; (lorazepam) 846-49-1; (oxycodone)
124-90-3, 76-42-6; (paracetamol) 103-90-2; (trazodone)
19794-93-5, 25332-39-2; (fentanyl) 437-38-7

CAS REGISTRY NO.:

FILE 'HOME' ENTERED AT 11:13:55 ON 14 DEC 2006

10/661458

SEARCH HISTORY

-> d his nofile

(FILE 'HOME' ENTERED AT 09:53:23 ON 14 DEC 2006)

FILE 'CAPLUS' ENTERED AT 09:53:50 ON 14 DEC 2006

D SAVED
ACT ARN458CAAUL/A

L1 1 SEA ABB-ON US2003-661458/APPS

L2 141 SEA ABB-ON PACE G7/AU

L3 11003 SEA ABB-ON SMITH M7/AU

L4 1 SEA ABB-ON L3 AND L3

D SCAN

FILE 'STINGUIDE' ENTERED AT 09:54:39 ON 14 DEC 2006

FILE 'REGISTRY' ENTERED AT 09:55:54 ON 14 DEC 2006

L5 1 SEA ABB-ON MORPHINE/CN

L6 1 SEA ABB-ON FENTANYL/CN

L7 1 SEA ABB-ON SUFFENTANIL/CN

L8 1 SEA ABB-ON ALFENTANYL/CN

L9 1 SEA ABB-ON OXYMORPHONE/CN

L10 1 SEA ABB-ON HYDROMORPHONE/CN

L11 1 SEA ABB-ON OXYCODONE/CN

FILE 'CAPLUS' ENTERED AT 09:56:07 ON 14 DEC 2006

L12 31087 SEA ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)

L13 1073 SEA ABB-ON L11

D SCAN L4

L14 12914 SEA ABB-ON OPIOIDS/CT

L15 1209 SEA ABB-ON L14(L)KAPPA/OBI

L16 1944 SEA ABB-ON L14(L)MU/OBI

L17 56591 SEA ABB-ON AGONISTS/OBI

L18 368 SEA ABB-ON L15(L)L17

L19 454 SEA ABB-ON L16(L)L17

L20 19117 SEA ABB-ON RESPIRATORY TRACT/OBI

L21 76 SEA ABB-ON L20(L)CARCINOMA/OBI

L22 25232 SEA ABB-ON ASTHMA/OBI

L23 424 SEA ABB-ON BRONCHIECTASIS/OBI OR BRONCHI?/OBI (L)DILATATION/OBI

OR KARTAGENER/OBI

L24 28786 SEA ABB-ON TUBERCULOSIS/OBI

L25 4089 SEA ABB-ON BRONCHITIS/OBI

L26 120 SEA ABB-ON RESPIRATORY SYSTEM, NEOPLASM/CT

L27 35560 SEA ABB-ON LUNG, NEOPLASM/CT

L28 4982 SEA ABB-ON CHRONIC OBSTRUCTIVE PULMONARY/OBI OR COPD/OBI

L29 7726 SEA ABB-ON BRONCHOPNEUMONIA/OBI OR PNEUMONIA/OBI

L30 136 SEA ABB-ON LARYNGITIS/OBI

L31 8101 SEA ABB-ON SINUSITIS/OBI

L32 2601 SEA ABB-ON EMPHYSEMA/OBI

L33 6378 SEA ABB-ON FIBROSINO/OBI (L)ALVEOLITIS/OBI OR (PULMONARY/OBI

OR LUNG/OBI OR RESPIRATORY/OBI) (L) (FIBROSIS/OBI OR SARCOIDOSIS/OBI)

L34 6 SEA ABB-ON SLEEP DISORDERS/CT (L)RESPIRATORY/OBI

L35 943 SEA ABB-ON SLEEP/OBI (L)APNEA/OBI

L36 1691 SEA ABB-ON SARCOIDOSIS/CT

L37 39125 SEA ABB-ON DRUG INTERACTIONS-OLD, WT/CT

L38 4450 SEA ABB-ON DRUG DELIVERY SYSTEMS-OLD/CT (L)COMB?/OBI

71

72

10/661458

L39 16989 SEA ABB-ON COMBINATION CHEMOTHERAPY/CT
L40 5480 SEA ABB-ON COMB7/OBI(L)PHARMAC7/OBI
L41 6 SEA ABB-ON (L12 OR L19) AND (L13 OR L18) AND (L21 OR L22 OR
L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR
L32 OR L33 OR L34 OR L35 OR L36) AND (L37 OR L38 OR L39 OR
L40)
L42 552 SEA ABB-ON (L12 OR L19) (L) (COMB7/OBI OR COADMIN7/OBI OR
CODRUG7/OBI OR CONCOMITANT7/OBI OR CONCURRENT7/OBI OR BLEND7/OB
I OR MIXTURE7/OBI)
L43 82 SEA ABB-ON (L13 OR L18) (L) (COMB7/OBI OR COADMIN7/OBI OR
CODRUG7/OBI OR CONCOMITANT7/OBI OR CONCURRENT7/OBI OR BLEND7/OB
I OR MIXTURE7/OBI)
L44 3 SEA ABB-ON L42 AND L43 AND (L21 OR L32 OR L23 OR L24 OR L25
OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34
OR L35 OR L36)
L45 5 SEA ABB-ON ((L42 AND L43) OR (L12 OR L19) AND (L13 OR L18)
AND (L37 OR L38 OR L39 OR L40))) AND (L2 OR L3)

FILE 'EMBASE' ENTERED AT 10:09:18 ON 14 DEC 2006
L46 83 SEA ABB-ON PACE G7/AU
L47 8120 SEA ABB-ON SMITH M7/AU
L48 53452 SEA ABB-ON MORPHINE/CT
E FENTANYL/CT
E E3-ALL
L49 26736 SEA ABB-ON FENTANYL/CT OR FENTANYL CITRATE/CT
E SUFENTANIL/CT
L50 4395 SEA ABB-ON SUFENTANIL/CT OR SUFENTANIL CITRATE/CT
E ALFENTANIL/CT
E E5-ALL
L51 4482 SEA ABB-ON ALFENTANIL/CT
E OXYMORPHONE/CT
L52 805 SEA ABB-ON OXYMORPHONE/CT
E HYDROMORPHONE/CT
L53 2957 SEA ABB-ON HYDROMORPHONE/CT
E OXYCODONE/CT
L54 3754 SEA ABB-ON OXYCODONE/CT
E ASTHMA-ALL/CT
L55 84233 SEA ABB-ON ASTHMA-NT/CT
E BRONCHIETASIS-ALL/CT
L56 4535 SEA ABB-ON BRONCHIETASIS-NT/CT
E PULMONARY TUBER/CT
E E4-ALL
E E2-ALL
L57 15140 SEA ABB-ON LUNG TUBERCULOSIS/CT
E COPD/CT
E E3-ALL
E E2-ALL
L58 26377 SEA ABB-ON CHRONIC OBSTRUCTIVE LUNG DISEASE/CT
E BRONCHITIS-ALL/CT
L59 22047 SEA ABB-ON BRONCHITIS-NT/CT
E BRONCHOPNEUMONIA-ALL/CT
L60 2275 SEA ABB-ON BRONCHOPNEUMONIA/CT
E LARYNGITIS-ALL/CT
L61 2500 SEA ABB-ON LARYNGITIS-NT/CT
E SINUSITIS-ALL/CT
L62 12991 SEA ABB-ON SINUSITIS-NT/CT
E EMPHYSEMA-ALL/CT
L63 13249 SEA ABB-ON EMPHYSEMA-NT/CT
E FIBROSING ALV/CT
E E4-ALL

73

10/661458

L64 2738 SEA ABB-ON FIBROSING ALVEOLITIS/CT
E PULMONARY FIBROSIS/CT
E E3-ALL
E E2-ALL
L65 19527 SEA ABB-ON LUNG FIBROSIS-NT/CT
E SARCOID/CT
E SARCOIDOSIS/CT
E E3-ALL
L66 11397 SEA ABB-ON SARCOIDOSIS/CT
E LUNG CANCER/CT
L67 91685 SEA ABB-ON LUNG CANCER-NT/CT
E SLEEP APNEA-ALL/CT
E E3-ALL
L68 11977 SEA ABB-ON SLEEP APNEA SYNDROME/CT
L69 20 SEA ABB-ON (L46 AND L47) OR ((L46 OR L47) AND (L48 OR L49 OR
L50 OR L51 OR L52 OR L53) AND L54)
L70 0 SEA ABB-ON (L46 AND L47)
L71 10397 SEA ABB-ON (L47 OR L48 OR L49 OR L50 OR L51 OR L52 OR
L53) (L) (CB OR IT)/CT
L72 493 SEA ABB-ON L54(L) (CB OR IT)/CT
L73 5 SEA ABB-ON L71 AND L72 AND (L46 OR L47)
L74 5 SEA ABB-ON (L46 AND L47) OR (L71 AND L72 AND (L46 OR L47))
D TRIAL 1-5
L75 38068 SEA ABB-ON DRUG POTENTIATION/CT
L76 1228 SEA ABB-ON MU OPIATE RECEPTOR AGONIST/CT
L77 949 SEA ABB-ON KAPPA OPIATE RECEPTOR AGONIST/CT
L78 208 SEA ABB-ON L76(L) (CB OR IT)/CT
L79 149 SEA ABB-ON L77(L) (CB OR IT)/CT
L80 10397 SEA ABB-ON (L48 OR L49 OR L50 OR L51 OR L52 OR L53) (L) (CB OR
IT)/CT
L81 5 SEA ABB-ON (L46 AND L47) OR (L80 AND L72 AND (L46 OR L47))
L82 0 SEA ABB-ON (L48 OR L49 OR L50 OR L51 OR L52 OR L53 OR L76)
AND (L77 OR L54) AND L75 AND (L55 OR L56 OR L57 OR L58 OR L59
OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR L66 OR L67 OR
L68)
L83 820 SEA ABB-ON (L72 OR L79) OR (L80 OR L78) AND (L55 OR L56 OR
L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR
L66 OR L67 OR L68)
L84 2 SEA ABB-ON (L72 OR L79) AND (L80 OR L78) AND (L55 OR L56 OR
L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR
L66 OR L67 OR L68)
D TRIAL 1-2

FILE 'DRUGU' ENTERED AT 10:26:08 ON 14 DEC 2006

L85 2 SEA ABB-ON PACE G7/AU
L86 1100 SEA ABB-ON SMITH M7/AU
D TRIAL L85 1-2
L87 9457 SEA ABB-ON (L5 OR L6 OR L7 OR L8 OR L9 OR L10)
L88 269 SEA ABB-ON L11
E MORPHINE/CT
L89 19705 SEA ABB-ON MORPHINE/CT
E FENTANYL/CT
L90 11240 SEA ABB-ON FENTANYL/CT
E SUFENTANIL/CT
L91 2280 SEA ABB-ON SUFENTANIL/CT
E ALFENTANIL/CT
L92 2680 SEA ABB-ON ALFENTANIL/CT
E OXYMORPHONE/CT
L93 252 SEA ABB-ON OXYMORPHONE/CT
E HYDROMORPHONE/CT

74

10/661458

L94 866 SEA ABB-ON HYDROMORPHONE/CT
E OXYCODONE/CT
L95 986 SEA ABB-ON OXYCODONE/CT
E OPIOID AGONIST/CT
L96 9 SEA ABB-ON (L85 AND L86) OR ((L85 OR L86) AND (L87 OR L89 OR
L90 OR L91 OR L92 OR L93 OR L94) AND (L88 OR L95))
L97 125676 SEA ABB-ON COMB./CT
L98 433001 SEA ABB-ON DRUG INTERACTIONS/CT
L99 88 SEA ABB-ON ((L97 OR L98) AND (L87 OR L89 OR L90 OR L91 OR L92
OR L93 OR L94) AND (L88 OR L95))
L100 31287 SEA ABB-ON ASTHMA OR BRONCHIETASIS OR BRONCHI7(2A)DILATATION
OR KARTAGENER OR TUBERCULOSIS
L101 3808 SEA ABB-ON COPD OR CHRONIC OBSTRUCTIVE (W) (LUNG OR PULMONARY
OR RESPIRATORY)
L102 24212 SEA ABB-ON BRONCHITIS OR BRONCHOPNEUMONIA OR PNEUMONIA OR
LARYNGITIS OR SINUSITIS OR EMPHYSEMA
L103 1971 SEA ABB-ON FIBROSING ALVEOLITIS OR FIBROSIS(A) (LUNG OR
PULMONARY OR RESPIRATORY)
L104 951 SEA ABB-ON SARCOIDOSIS
L105 17785 SEA ABB-ON (LUNG OR PULMONARY OR RESPIRATORY) (2A) (CANCER# OR
NEOPLAS7 OR CARCINOMA#)
L106 433 SEA ABB-ON SLEEP APNEA
L107 4 SEA ABB-ON ((L97 OR L98) AND (L87 OR L89 OR L90 OR L91 OR L92
OR L93 OR L94) AND (L88 OR L95)) AND (L100 OR L101 OR L102 OR
L103 OR L104 OR L105 OR L106)
D TRIAL 1-4

FILE 'STNGUIDE' ENTERED AT 10:34:45 ON 14 DEC 2006

FILE 'WPIX' ENTERED AT 10:36:41 ON 14 DEC 2006

L108 79 SEA ABB-ON PACE G7/AU
L109 2413 SEA ABB-ON SMITH M7/AU
L110 1 SEA ABB-ON L108 AND L109
D TRIAL

FILE 'STNGUIDE' ENTERED AT 10:37:23 ON 14 DEC 2006

FILE 'WPIX' ENTERED AT 10:38:56 ON 14 DEC 2006

E B04-A04-ALL/MC
E B07-H-ALL/MC
E B12-M10A-ALL/MC
E B12-M10C-ALL/MC
E B14-C01-ALL/MC
E B14-H01-ALL/MC
E B14-H01N-ALL/MC
E B14-J02-ALL/MC
E B14-K01-ALL/MC
E B14-L01-ALL/MC
E B14-S09-ALL/MC

FILE 'STNGUIDE' ENTERED AT 10:39:14 ON 14 DEC 2006

FILE 'WPIX' ENTERED AT 10:41:48 ON 14 DEC 2006

L111 3147 SEA ABB-ON MORPHINE/B1,ABEX OR FENTANYL/B1,ABEX OR ALFENTANIL/
B1,ABEX OR SUFENTANIL/B1,ABEX OR OXYMORPHONE/B1,ABEX OR
MRZ2593/B1,ABEX OR MRZ 2593/B1,ABEX OR HYDROMORPHONE/B1,ABEX
E OXYCODONE/CN
L112 4 SEA ABB-ON OXYCODONE7/CN
L113 431 SEA ABB-ON L112/DCR
SEL L112 SDR#,SDCH,DCSE

75

10/661458

L114 4 SEA ABB-ON (RABAGO/SDCN OR RACDH7/SDCN OR RA0FC0/SDCN OR
RD6854/SDCN OR R16303/SDCN OR 103043-1-1-0/DCSE OR 103043-1-1-0
/DCSE OR 103043-1-2-0/DCSE OR 758270-1-0-0/DCSE)
L115 435 SEA ABB-ON L114 OR L113
L116 513 SEA ABB-ON OXYCODONE/B1,ABEX
L117 198 SEA ABB-ON MU OPIOIDS/B1,ABEX
L118 186 SEA ABB-ON KAPPA/B1,ABEX (1W) OPIOIDS/B1,ABEX
L119 12146 SEA ABB-ON B14-L01/MC OR C14-L01/MC
L120 100 SEA ABB-ON L117(2A)AGONISTS/B1,ABEX OR (L117 AND L119)
L121 102 SEA ABB-ON L118(2A)AGONISTS/B1,ABEX OR (L118 AND L119)
L122 486502 SEA ABB-ON (H782 OR P667)/MO,M1,M2,M3,M4,M5,M6 OR A61K045/IPC
OR B12-C09 OR C12-C09 OR B14-S09 OR C14-S09/MC
L123 4 SEA ABB-ON (L108 OR L109) AND (L111 OR L120) AND (L115 OR
L116 OR L121) AND L122
L124 28604 SEA ABB-ON ASTHMA/B1,ABEX OR BRONCHIETASIS/B1,ABEX OR
BRONCHI7/B1,ABEX (2A)DILATATION/B1,ABEX OR KARTAGENER/B1,ABEX
OR TUBERCULOSIS/B1,ABEX
L125 5007 SEA ABB-ON COPD/B1,ABEX OR CHRONIC OBSTRUCTIVE/B1,ABEX (W) (LUNG
/B1,ABEX OR PULMONARY/B1,ABEX OR RESPIRATORY/B1,ABEX)
L126 11360 SEA ABB-ON BRONCHITIS/B1,ABEX OR BRONCHOPNEUMONIA/B1,ABEX OR
PNEUMONIA/B1,ABEX OR LARYNGITIS/B1,ABEX OR SINUSITIS/B1,ABEX
OR EMPHYSEMA/B1,ABEX
L127 2462 SEA ABB-ON FIBROSING ALVEOLITIS/B1,ABEX OR FIBROSIS/B1,ABEX (A)
(LUNG/B1,ABEX OR PULMONARY/B1,ABEX OR RESPIRATORY/B1,ABEX)
L128 3624 SEA ABB-ON SARCOIDOSIS/B1,ABEX OR SLEEP APNEA/B1,ABEX
L129 8806 SEA ABB-ON (LUNG/B1,ABEX OR PULMONARY/B1,ABEX OR RESPIRATORY/B
1,ABEX) (2A) (CANCER#/B1,ABEX OR NEOPLAS7/B1,ABEX OR CARCINOMA#/B
1,ABEX)
L130 26 SEA ABB-ON (L111 OR L120) AND (L115 OR L116 OR L121) AND L122
AND (L124 OR L125 OR L126 OR L127 OR L128 OR L129)
L131 25 SEA ABB-ON L130 NOT (L110 OR L123)
D TRIAL 1-8
L132 20 SEA ABB-ON SUBANALGES7/B1,ABEX OR SUB ANALGES7/B1,ABEX
L133 1 SEA ABB-ON L132 AND L130
D TRIAL
D KWIC L131 6-10
D KWIC L131 11-13

FILE 'WPIX' ENTERED AT 10:55:27 ON 14 DEC 2006

D KWIC L131 11-13

FILE 'WPIX' ENTERED AT 10:56:51 ON 14 DEC 2006

L134 1 SEA ABB-ON L120 AND L121 AND L122 AND (L124 OR L125 OR L126
OR L127 OR L128 OR L129)
L135 20 SEA ABB-ON L115 AND L111 AND L122 AND (L124 OR L125 OR L126
OR L127 OR L128 OR L129)
D KWIC L133
L136 299 SEA ABB-ON ((L111 OR L117)) (5A) ((L116 OR L121)) (5A) (COMB7/B1,AB
EX OR CODRUG7/B1,ABEX OR COADMIN7/B1,ABEX OR CONCOMITANT7/B1,ABEX)
OR CONCURRENT7/B1,ABEX OR BLEND7/B1,ABEX OR MIX7/B1,ABEX)
L137 18 SEA ABB-ON L136 AND L122 AND (L124 OR L125 OR L126 OR L127 OR
L128 OR L129)
D QUS
L138 84 SEA ABB-ON L118(2A)AGONISTS/B1,ABEX
L139 61 SEA ABB-ON L117(2A)AGONISTS/B1,ABEX
L140 384 SEA ABB-ON ((L111 OR L139)) (5A) ((L116 OR L138))
L141 10 SEA ABB-ON L140(5A) (COMB7/B1,ABEX OR CODRUG7/B1,ABEX OR
COADMIN7/B1,ABEX OR CONCOMITANT7/B1,ABEX OR CONCURRENT7/B1,ABEX
OR BLEND7/B1,ABEX OR MIX7/B1,ABEX)
L142 2 SEA ABB-ON L141 AND (L124 OR L125 OR L126 OR L127 OR L128 OR

76

10/661458

L143 1129) 25 SEA ABB-ON L140 AND L122 AND (L124 OR L125 OR L126 OR L127 OR L128 OR L129)

FILE 'MEDLINE' ENTERED AT 11:04:27 ON 14 DEC 2006

D SAVED

ACT ARN458MEDAU/A

L144(94)SEA FILE-MEDLINE ABB-ON PACE G7/AU

L145(10732)SEA FILE-MEDLINE ABB-ON SMITH M7/AU

L146(0)SEA FILE-MEDLINE ABB-ON L144 AND L145

L147(28104)SEA FILE-MEDLINE ABB-ON MORPHINE/CT

L148(10382)SEA FILE-MEDLINE ABB-ON FENTANYL-NT/CT

L149(294)SEA FILE-MEDLINE ABB-ON OXYMORPHONE/CT

L150(704)SEA FILE-MEDLINE ABB-ON HYDROMORPHONE/CT

L151(540)SEA FILE-MEDLINE ABB-ON OXYCODONE/CT

L152(124991)SEA FILE-MEDLINE ABB-ON LUNG DISEASES, OBSTRUCTIVE-NT/CT

L153(5936)SEA FILE-MEDLINE ABB-ON BRONCHIECTASIS-NT/CT

L154(57086)SEA FILE-MEDLINE ABB-ON TUBERCULOSIS, PULMONARY-NT/CT

L155(3460)SEA FILE-MEDLINE ABB-ON BRONCHOPNEUMONIA/CT

L156(3610)SEA FILE-MEDLINE ABB-ON LARYNGITIS-NT/CT

L157(11628)SEA FILE-MEDLINE ABB-ON SINUSITIS-NT/CT

L158(13172)SEA FILE-MEDLINE ABB-ON PULMONARY FIBROSIS/CT

L159(1561)SEA FILE-MEDLINE ABB-ON SARCOIDOSIS, PULMONARY/CT

L160(113814)SEA FILE-MEDLINE ABB-ON LUNG NEOPLASMS-NT/CT

L161(12706)SEA FILE-MEDLINE ABB-ON SLEEP APNEA SYNDROMES-NT/CT

L162(0)SEA FILE-MEDLINE ABB-ON (L144 OR L145) AND (L147 OR L148 OR L1

L163 0 SEA ABB-ON L146 OR L162

ACT ARN458MED1/A

L164(28104)SEA FILE-MEDLINE ABB-ON MORPHINE/CT

L165(10382)SEA FILE-MEDLINE ABB-ON FENTANYL-NT/CT

L166(294)SEA FILE-MEDLINE ABB-ON OXYMORPHONE/CT

L167(704)SEA FILE-MEDLINE ABB-ON HYDROMORPHONE/CT

L168(540)SEA FILE-MEDLINE ABB-ON OXYCODONE/CT

L169(124991)SEA FILE-MEDLINE ABB-ON LUNG DISEASES, OBSTRUCTIVE-NT/CT

L170(5936)SEA FILE-MEDLINE ABB-ON BRONCHIECTASIS-NT/CT

L171(57086)SEA FILE-MEDLINE ABB-ON TUBERCULOSIS, PULMONARY-NT/CT

L172(3460)SEA FILE-MEDLINE ABB-ON BRONCHOPNEUMONIA/CT

L173(3610)SEA FILE-MEDLINE ABB-ON LARYNGITIS-NT/CT

L174(11628)SEA FILE-MEDLINE ABB-ON SINUSITIS-NT/CT

L175(13172)SEA FILE-MEDLINE ABB-ON PULMONARY FIBROSIS/CT

L176(1561)SEA FILE-MEDLINE ABB-ON SARCOIDOSIS, PULMONARY/CT

L177(113814)SEA FILE-MEDLINE ABB-ON LUNG NEOPLASMS-NT/CT

L178(12706)SEA FILE-MEDLINE ABB-ON SLEEP APNEA SYNDROMES-NT/CT

L179 1 SEA ABB-ON (L164 OR L165 OR L166 OR L167) AND L168 AND (L169 OR L170 OR L171 OR L172 OR L173 OR L174 OR L175 OR L176 OR L177 OR L178)

ACT ARN458MED2/A

L180(28104)SEA FILE-MEDLINE ABB-ON MORPHINE/CT

L181(10382)SEA FILE-MEDLINE ABB-ON FENTANYL-NT/CT

L182(294)SEA FILE-MEDLINE ABB-ON OXYMORPHONE/CT

L183(704)SEA FILE-MEDLINE ABB-ON HYDROMORPHONE/CT

L184(540)SEA FILE-MEDLINE ABB-ON OXYCODONE/CT

L185(108974)SEA FILE-MEDLINE ABB-ON DRUG INTERACTIONS-NT/CT

L186(42787)SEA FILE-MEDLINE ABB-ON DRUG COMBINATIONS/CT

L187(97253)SEA FILE-MEDLINE ABB-ON DRUG THERAPY, COMBINATION/CT

77

10/661458

L188(15)SEA FILE-MEDLINE ABB-ON (L180 OR L181 OR L182 OR L183) AND L18

L189 3 SEA ABB-ON L188 AND SYNERG?

ACT ARN458MED3/A

L190(108974)SEA FILE-MEDLINE ABB-ON DRUG INTERACTIONS-NT/CT

L191(42787)SEA FILE-MEDLINE ABB-ON DRUG COMBINATIONS/CT

L192(97253)SEA FILE-MEDLINE ABB-ON DRUG THERAPY, COMBINATION/CT

L193(1136)SEA FILE-MEDLINE ABB-ON RECEPTORS, OPIOID, MU/CT(L)AG/CT

L194(881)SEA FILE-MEDLINE ABB-ON RECEPTORS, OPIOID, KAPPA/CT(L)AG/CT

L195(23)SEA FILE-MEDLINE ABB-ON L193 AND L194 AND (L198 OR L199 OR L19

L196(240557)SEA FILE-MEDLINE ABB-ON DOSE-RESPONSE RELATIONSHIP, DRUG/CT

L197 1 SEA ABB-ON L195 AND L196 AND CONDITIONING, OPERANT/CT

ACT ARN458MED4/A

L198(28104)SEA FILE-MEDLINE ABB-ON MORPHINE/CT

L199(10382)SEA FILE-MEDLINE ABB-ON FENTANYL-NT/CT

L200(294)SEA FILE-MEDLINE ABB-ON OXYMORPHONE/CT

L201(704)SEA FILE-MEDLINE ABB-ON HYDROMORPHONE/CT

L202(540)SEA FILE-MEDLINE ABB-ON OXYCODONE/CT

L203(1136)SEA FILE-MEDLINE ABB-ON RECEPTORS, OPIOID, MU/CT(L)AG/CT

L204(881)SEA FILE-MEDLINE ABB-ON RECEPTORS, OPIOID, KAPPA/CT(L)AG/CT

L205(488)SEA FILE-MEDLINE ABB-ON (L198 OR L199 OR L200 OR L201 OR L203)

L206(8267)SEA FILE-MEDLINE ABB-ON COUGH/CT

L207 1 SEA ABB-ON L205 AND L206

FILE 'STNGUIDE' ENTERED AT 11:05:43 ON 14 DEC 2006

FILE 'CAPLUS' ENTERED AT 11:06:43 ON 14 DEC 2006

D QUE L1

D QUE L45

L208 5 SEA ABB-ON (L1 OR L45)

FILE 'EMBASE' ENTERED AT 11:06:46 ON 14 DEC 2006

D QUE L81

FILE 'DRUGU' ENTERED AT 11:06:47 ON 14 DEC 2006

D QUE L96

FILE 'WPIX' ENTERED AT 11:06:48 ON 14 DEC 2006

D QUE L110

D QUE L123

FILE 'MEDLINE' ENTERED AT 11:06:50 ON 14 DEC 2006

D QUE L163

FILE 'DRUGU, CAPLUS, EMBASE' ENTERED AT 11:07:13 ON 14 DEC 2006

L209 15 DUP REM L96 L208 L81 (4 DUPLICATES REMOVED)

ANSWERS '1-9' FROM FILE DRUGU

ANSWERS '10-13' FROM FILE CAPLUS

ANSWERS '14-15' FROM FILE EMBASE

D IBIB ED ABS 1-15

FILE 'STNGUIDE' ENTERED AT 11:07:44 ON 14 DEC 2006

FILE 'CAPLUS' ENTERED AT 11:10:12 ON 14 DEC 2006

D QUE L1

D QUE L45

78

10/661458

L210 5 SEA ABB-ON (L1 OR L45)

FILE 'EMBASE' ENTERED AT 11:10:14 ON 14 DEC 2006

D QUE L81

FILE 'DRUGU' ENTERED AT 11:10:15 ON 14 DEC 2006

D QUE L96

FILE 'WPIX' ENTERED AT 11:10:16 ON 14 DEC 2006

D QUE L110

D QUE L123

L211 4 SEA ABB-ON (L110 OR L123)

FILE 'MEDLINE' ENTERED AT 11:10:19 ON 14 DEC 2006

D QUE L163

FILE 'DRUGU, CAPLUS, WPIX, EMBASE' ENTERED AT 11:10:37 ON 14 DEC 2006

L212 16 DUP REM L96 L210 L211 L81 (7 DUPLICATES REMOVED)

ANSWERS '1-9' FROM FILE DRUGU

ANSWERS '10-13' FROM FILE CAPLUS

ANSWER '14' FROM FILE WPIX

ANSWERS '15-16' FROM FILE EMBASE

D IBIB ED ABS 1-16

FILE 'STNGUIDE' ENTERED AT 11:11:03 ON 14 DEC 2006

FILE 'CAPLUS' ENTERED AT 11:12:31 ON 14 DEC 2006

D QUE L41

D QUE L44

L213 5 SEA ABB-ON (L41 OR L44) NOT L210

FILE 'EMBASE' ENTERED AT 11:12:33 ON 14 DEC 2006

D QUE L82

D QUE L84

L214 2 SEA ABB-ON L84 NOT L81

FILE 'DRUGU' ENTERED AT 11:12:35 ON 14 DEC 2006

D QUE L107

L215 4 SEA ABB-ON L107 NOT L96

FILE 'WPIX' ENTERED AT 11:12:38 ON 14 DEC 2006

D QUE L134

D QUE L142

L216 2 SEA ABB-ON (L134 OR L142) NOT L211

FILE 'MEDLINE' ENTERED AT 11:12:43 ON 14 DEC 2006

D QUE L189

D QUE L197

D QUE L207

D QUE L179

L217 6 SEA ABB-ON (L189 OR L197 OR L207 OR L179)

FILE 'MEDLINE, DRUGU, CAPLUS, WPIX, EMBASE' ENTERED AT 11:13:15 ON 14 DEC 2006

L218 19 DUP REM L217 L215 L213 L216 L314 (0 DUPLICATES REMOVED)

ANSWERS '1-6' FROM FILE MEDLINE

ANSWERS '7-10' FROM FILE DRUGU

ANSWERS '11-15' FROM FILE CAPLUS

ANSWERS '16-17' FROM FILE WPIX

ANSWERS '18-19' FROM FILE EMBASE

79

10/661458

D IALL 1-10

D IBIB ED ABS HIT 11-15

D IBIB ABOQ TECH HITSTR 16-17

D IALL 18-19

FILE 'HOME' ENTERED AT 11:13:55 ON 14 DEC 2006

80